use of a Bayesian statistical framework provided a means of overcoming the above limitations.

b. Bayesian Approach. A Bayesian analysis allows the logical combination of two forms of information: ''prior knowledge'' about parameter values drawn from the scientific literature, and data from experimental studies (e.g., the mouse gas uptake studies, or, for humans, the open chamber experiments performed by Dow Chemical company), all within the context of a PBPK model. Clearly, neither prior information about parameter values nor experimental data alone are capable of precisely determining all parameter values in the PBPK model. If prior information were sufficient, the additional experiments performed by Clewell et al. and Dow Chemical Co. would not have had to be done. But the available experimental data alone are insufficient to pin down all parameters of the model to reasonable values (which is why no attempt was made to simultaneously optimize all PBPK parameters to data). Fitting only two or three parameters while holding others constant so as to reduce dimensionality leads to the biases and underestimation of variance mentioned above.

A second feature of this Bayesian approach is that it yields distributions for all of the PBPK model parameters together with information about their entire joint covariance structure. Thus, the Bayesian analysis outputs distributions of parameter values that are consistent with both all the available data as well as the prior information. It is then possible to use samples from the joint posterior distribution of the parameters to simulate formation of GST metabolites in lung tissue from different species and cancer risk, therefore producing posterior distributions for these endpoints. It should be noted that if no data are available (or if the data are not informative as to the likely value of the parameter), the posterior distribution is equivalent to the prior distribution and this approach is then equivalent to the standard Monte Carlo sampling from the prior distribution, as in Clewell et al. Alternately, Bayesian updating with a uniform prior distribution (i.e., complete ignorance about plausible values) used in conjunction with data leads to a posterior distribution proportional to the distribution of the data. The most important applications of the Bayesian approach arise when informative (e.g., physiological, anatomical) prior distributions exist, in parallel with experimental metabolic data. This is now the case with PBPK modeling of MC. In this case, Bayesian modeling results in all the information content of both prior distributions of parameter values and metabolic data being incorporated in the posterior distribution of parameter values, which will have reduced variance compared to the prior distribution. Distributions of parameter values for both human and mouse PBPK models, and the multistage cancer model, were determined with this technique.

c. PBPK Model Modifications. OSHA's final risk estimates were based on the Bayesian analysis described here. The Clewell model formed the structural core of the analysis, although five additional structural modifications were made as described below. These modifications were necessary to make the PBPK model more physiologically realistic:

(1) Bone marrow was treated as a separate compartment. In the Clewell model (as in many PBPK models), bone marrow tissue was combined with other tissues into a (presumably) kinetically homologous compartment. Based on blood perfusion rates, a reasonable choice would be to place marrow in the well-perfused tissue compartment. However, if the physicochemical affinity of the compartment is considered, it makes more sense to place marrow in the adipose tissue compartment, since red marrow (at least in humans) has a fat content of about 40% and yellow marrow has a fat content of 80%. In comparison, liver, brain, kidney and heart all have fat contents (in humans) well under 20% . In addition, bone marrow accounts for a significant percentage of body weight and receives a substantial fraction of cardiac output. Therefore, a strong argument can be made for treating bone marrow as a separate compartment, as OSHA has done here.

(2) Partitioning MFO and GST metabolism between the lung and liver. Clewell made the MFO and GST metabolic constants for lung dependent on the fitted constants for the liver, so as to reduce the number of fitted parameters to be simultaneously estimated from rodent and human *in vivo* data. For example, A1 is defined as the ratio of lung to liver *in vitro* MFO enzymatic activity, normalized to microsomal protein,

$$A1 = \frac{\text{nmol DCM oxidized/min/mg lung microsomal protein}}{\text{nmol DCM oxidized/min/mg liver microsomal protein}}$$

Similarly, A2 is the ratio of lung to liver *in vitro* GST enzymatic activity, normalized to cytosolic protein,

$$A2 = \frac{\text{nmol DCM conjugated/min/mg lung cytosolic protein}}{\text{nmol DCM conjugated/min/mg liver cytosolic protein}}$$

This assumes that lung and liver have equivalent mg protein per mg tissue contents. Yet the data of Litterst et al. (1973) argue against such an assumption. Litterst et al. measured microsomal protein and soluble protein in lung and liver tissues of mice, rats, hamsters, guinea pigs and rabbits. These data indicated ratios of mg microsomal protein content of lung versus liver tissue of less than 0.3, and a similar ratio for soluble protein of about 0.7. Thus, some adjustment of the constants A1 and A2 are required.

The equations used to compute a lung Vmax for the MFO pathway and a lung Kf for the GST pathway from a liver Vmax and Kf were thus modified to include an additional proportionality factor to account for differences in microsomal and cytosolic protein content of lung and liver tissue. Specifically,

$$Vmax_{lung.MFO} = Vmax_{liver.MFO} \times [V_{lung} / V_{liver}] \times A1 \times B1$$

where B1 is the ratio of [mg microsomal protein per mg of lung tissue] to the same measure for liver tissue. A geometric mean and geometric standard deviation for B1 were derived from the data of Litterst et al. (1973) to use as input in the Bayesian prior distribution for this parameter. Notably, accounting for this difference in protein content leads to a proportionality factor approximately four-fold less than that used by the Clewell et al. (i.e., A1 x B1 = 0.41 × 0.27 = 0.11).

Similarly, for $Kf_{lung.GST}$,

$$Kf_{lung.GST} = Kf_{liver.GST} \times A2 \times B2$$

Here too, the data of Litterst et al. (1973) were used to compute a ratio of mg soluble protein per mg lung to the same measure for liver, yielding a mean value of 0.68 for B2. For a human B2, the average of the ratios computed for mice, rats, hamsters, guinea pigs, and rabbits as per Litterst et al. (1973) was used.

(3) Linkage of alveolar ventilation to cardiac output. In recognition of OSHA's interest in occupational exposures, Clewell used values of cardiac output and alveolar ventilation rates consistent with the performance of light work. However, they did not account for the altered distribution of regional blood flows known to occur in response to increases in work intensity [Exs. 7–115, 7–120, 21–81], as was done in subsequent MC PBPK work by Dankovic and Bailer [Ex. 23–18] (1994). In the latter analysis, alveolar ventilation (QP) was made dependent on cardiac output (QC) by making QP = QC × VPR, where VPR is the ventilation-perfusion ratio. VPR was treated as a random variable with an assigned prior probability distribution.

(4) Linkage of work intensity to changes in physiology. Cardiac output, ventilation perfusion ratio, and percent of cardiac output delivered to tissues were made dependent on work intensity. Using the data of Åstrand (1983) [Ex. 21–81]—and similar to what was done by Dankovic and Bailer (1994) [Ex. 23–18]—slope factors were derived to describe change in flows per change in work intensity as measured in watts. These slope factors were then used to modify resting flows for varying levels of work intensity. This approach was taken so that the influence of variability in work load (i.e, work load was treated as a random variable)—with concomitant adjustments to regional blood flows and ventilation rate—on delivered dose could be modeled.

(5) Maintaining mass balance in sampling of fractional blood flows and compartment volumes. Monte Carlo sampling of fractional quantities such as the proportion of cardiac output delivered to different compartments, or the proportion of body weight represented by a given compartment, requires the imposition of some type of constraint to prevent random sampling leading to summed proportions greater than the whole (and thus causing nonsensical departures from mass balance). The following constraint was imposed: VppC = 0.82—∑ViC 's (0.82 is a nominal value for the fraction of body weight absent bone, blood, and stomach and intestinal contents), QwpC = 1—∑QiC 's (in the mouse model), and QppC = 1—∑QiC 's (in the human model). The use of either QwpC or QppC as the quantity to be made dependent on the other fractional flows has biological appeal—one expects that higher fractional blood flow to the poorly-perfused compartment (i.e., muscle and skin) should be accompanied by a lower fractional flow to the well-perfused compartment, and vice versa. The choice of QwpC versus QppC as the one to be made dependent on others appeared to be unimportant in work with the mouse model. The choice was important in work with the human model. Here it was necessary to choose QppC, because of its large variance relative to QwpC (i.e., since QppC cannot be estimated precisely, it makes sense to let our greater knowledge of the other fractional flows inform us about plausible values of QppC).

The above approach modifies the approach taken by Clewell et al. [Ex. 96]. Their approach was to randomly draw from the distributions for cardiac output and all fractional flows, use the random draws to compute the absolute flows to the individual compartments, and then to sum the individual flows to make a new cardiac output value for use in the simulation. On the other hand, OSHA's final analysis avoided arbitrarily modifying the prior distribution for cardiac output (which happens to be one of the relatively well-known parameters). Furthermore, Clewell did not make the fractional flows dependent on one another.

d. Prior Probability Distributions. A skewed, lognormal-like distribution is generally observed for biological parameters. However, most, if not all, parameters are also positive and have physiological bounds. Thus, truncated lognormal distributions of the parameter values were used in this analysis. They do not differ appreciably from normal distributions for small values of the variance.

In specifying prior distributions an attempt was made to characterize the variability of the mean parameter values for small groups of rodents and humans. This focus was adopted to make the prior distribution congruent with the data sets available for Bayesian analysis. For example, the rodent gas uptake data represent the aggregate pharmacokinetic behavior of groups of 5 mice. Prior distributions were therefore constructed to reflect the degree of variability in mean physiological and anatomical PBPK parameters for small groups of mice. A similar approach was taken in defining prior distributions for human physiologic and anatomic parameters, since the available experimental data reflected the averaged pharmacokinetic behavior of 6 subjects. In practice, this meant amassing studies reporting mean values for certain PBPK parameters (e.g., tissue weights, blood flows, cardiac output, minute ventilation), and then using these means as data for computing a geometric mean (GM) and geometric standard deviation (GSD) with which to estimate the parameter values for the truncated lognormal distributions. Sampling of all lognormal distributions was truncated at 2 GSDs, with one exception. Truncation of the blood:air partition coefficient was extended to 3 GSDs based on results from preliminary runs.

Table VI–5 presents a summary of the prior probability distributions used in the Bayesian fitting of the mouse and human data sets. The prior distributions for metabolic constants to be estimated from *in vivo* data were made very broad (i.e., assigned a GSD of 10) to reflect our ignorance of these values before examining the data. Similarly, the prior distributions for parameters of the multistage cancer model were broad uniform distributions, constrained to be positive, as required by the standard model.

TABLE VI–5.—PRIOR DISTRIBUTIONS USED IN BAYESIAN ANALYSIS OF MOUSE AND HUMAN IN-VIVO DATA

	Parameter	Mouse priors		Human priors	
		GM	GSD	GM	GSD
Flows:					
QCC	Cardiac Output (l/hr/kg—BW)	a 34.8	1.14	4.2	1.10
VPR	Alveolar Ventilation Perfusion Rate	b 1.22	1.95	1.35	1.15
Tissue Blood Flows (fraction of cardiac output):					
QgiC	GI Tract	0.165	1.30	0.191	1.25
QliC	Liver	0.017	1.20	0.067	1.20
QfatC	Fat	0.047	1.60	0.057	1.45
QppC	Poorly Perfused Tissues	0.276	1.25	0.198 c	1.55
QwpC	Well Perfused Tissues	c 0.369	1.10	0.443	1.25
QmarC	Bone Marrow	0.089	1.60	0.044	1.70
Tissue Volumes (fraction of body weight):					
VgiC	GI Tract	0.035	1.30	0.017	1.10
VliC	Liver	0.045	1.20	0.026	1.10
VfatC	Fat	0.077	1.40	0.204	1.20
VppC	Poorly Perfused Tissues	c 0.556	1.10	0.470 c	1.15
VwpC	Well Perfused Tissues	0.065	1.15	0.044	1.10
VluC	Lung	0.008	1.30	0.008	1.15
VmarC	Bone Marrow	0.033	1.50	0.050	1.10
Equilibrium Partition Coefficients:					
Pblo	Blood:Air	13.7	1.80	8.4	1.30
Pgi	GI Tract:Air	10.5	1.20	8.1	1.60
Pli	Liver:Air	22.9	2.00	9.9	1.60
Pfat	Fat:Air	98.2	1.40	97.6	1.25
Ppp	Poorly Perfused Tissues:Air	9.5	1.30	6.8	1.60
Pwp	Well Perfused Tissues:Air	10.2	1.20	7.6	1.40
Plu	Lung:Air	10.0	1.30	7.6	1.50
Pmar	Bone Marrow:Air	62.0	1.60	48.8	1.60
Metabolic Parameters:					
VmaxC	Maximum metabolic velocity of MFO saturable pathway (mg/hr/kg—liver).	750	10.00	75	10.00
KM	Affinity of MFO saturable pathway (mg/l)	1.35	10.00	0.6	10.00
KFC	First order rate constant for GST pathway (l/hr/kg − 0.25).	1.5	10.00	Mouse post. d	Mouse post. d
A1	Ratio of lung to liver in-vitro MFO metabolic velocities (nmol/min/gm—lung—micros.Prot)/ (nmol/min/gm—liver—micros.Prot).	0.405	1.67	0.0045	4.50
A2	Ratio of lung to liver in-vitro GST metabolic velocities (nmol/min/gm—lung—cytos.Prot)/ (nmol/min/gm—liver—cytos.Prot).	0.282	1.67	0.122	3.60
B1	Ratio of lung and liver tissue content of microsomal protein.	0.271	1.25	0.297	1.10
B2	Ratio of lung and liver tissue content of cytosolic protein.	0.721	1.25	0.807	1.20
Sp—Kf	Allometric scaling power for body weight scaling of KFC from mice to humans.			−0.272 e	0.08 e

Notes: (a) value computed for 0.025 kg mouse, 70 kg human; (b) unitless; (c) prior distribution not used, fractional flow made functionally dependent on others (see text); (d) human prior set equal to mouse posterior; (e) mean and standard deviation of a truncated normal distribution.

While it is desirable to separate variability into components reflecting pure uncertainty (e.g., measurement error) versus interindividual heterogeneity and to propagate them separately, it is necessary to build from the start an adequate statistical model. The problem here is complicated by the fact that both the rodent and human *in vivo* data used for estimating metabolic constants reflected either aggregated or averaged pharmacokinetic behavior. Thus the prior distributions and the statistical model used here aggregate variability due to both finite precision in measured values and heterogeneity among average values for small groups of rodents or humans; they do not, it must be emphasized, reflect heterogeneity among the individual humans in a large, representative population.

e. In Vivo Rodent and Human data. Bayesian updating of the distributions was performed using the same data sets used by Clewell et al. to obtain fitted estimates of mouse and human metabolic constants; namely, gas uptake studies with mice with or without pretreatment with a MFO inhibitor and the human open chamber inhalation studies. All mouse gas uptake studies were conducted with 5 female mice in

a single chamber. Thus, measured observations of decline in chamber concentration of MC represent the aggregate pharmacokinetic behavior of groups of 5 animals.

The human *in vivo* data were obtained from Tables 2 and 3 in Andersen et al. (1991) [Ex. 21–94]. Briefly, these data represent exhaled breath and venous blood concentrations of MC for 6 male human volunteers exposed to MC concentrations of 100 or 350 ppm for a period of 6 hours. These data have only been reported as means and standard deviations of the six subjects, which is unfortunate. Thus, the available data reflect the average pharmacokinetic behavior of the 6 subjects. When simulating the human data reported in Andersen et al. (1991), the work load was assumed to be zero watts (rest) and the averaged body weight of the 6 subjects was assumed to be known without error (86 kg).

f. Simulating the Rodent Bioassay and Human Occupational Exposure. Distributions for GST metabolism in the lungs of mice exposed to 2000 ppm or 4000 ppm exposures, for 6 hrs/day and 5 days/week, were obtained by simulating these two exposures (the ones used in the NTP bioassay) with 5000 realizations drawn from the joint posterior distribution of the mouse PBPK parameters.

The quantity of metabolites formed during the 4th week (dynamic equilibrium reached) was divided by 7 to give an average measure per day. For use as an input dose to the multistage model, these posterior distributions were approximated by truncated lognormals.

The same set of 5000 parameter vectors was used to simulate both 2000 and 4000 ppm MC exposures. The control dose was always assumed to be 0. Thus, a 5000-by-3 matrix of doses was generated, where the three column vectors represent different realizations of a particular dose group (0, 2000 and 4000 ppm MC) and the row vectors represent different realizations of bioassay doses.

This method of using the joint posterior distributions for the two doses in the mouse bioassay implies certain assumptions about the uncertainties. Most importantly, this approach (referred to in this document as the ''dependence case'') assumes that the posterior distributions primarily reflect uncertainty about a single average value equally applicable to all groups of approximately 50 mice (i.e., it assumes groups of 50 mice will have the same ''average'' physiological, anatomical, physicochemical and metabolic attributes, and that these average values are simply known to us with uncertainty). An alternative would be to model the ''independence case'' by using a different random draw from the vector of PBPK parameters for one dose group than for the other. This approach assumes that the posterior distributions primarily reflect heterogeneity in the average attributes of groups of 50 rodents. Under the dependence case, estimates of metabolized dose for the two exposures would tend to move in tandem for a given simulation (i.e., when one dose is estimated to be low relative to its average, so is the other; likewise, when one is high, so is the other), and in principle would therefore exhibit less variability in dose-response shape (e.g., linear, sublinear, supralinear).

It appears that the dependence case is more reasonable than the independence case, by appealing to biological theory and by examining the results of the sensitivity analysis conducted as part of this risk assessment. The sensitivity analysis showed that predicted mouse GST metabolism at 2000 ppm was most sensitive to variation in the model parameter A2. Variability in A2 was primarily a consequence of uncertainty in using an *in vitro* ratio of enzymatic activity to make inferences about an *in vivo* ratio. Therefore, uncertainty rather than heterogeneity seems to dominate the distribution of mouse GST metabolism estimates. Besides, laboratory rodents have a carefully controlled genetic makeup, primarily so that they will differ little from each other physiologically; thus, groups of 50 rodents should have extremely similar average characteristics (the variance of the mean of a characteristic within a group of 50 rodents will be approximately 50 times smaller than the (already small) inter-individual variance). OSHA has determined that this reasoning supports use of the dependence case in this analysis. (Note that the excess risk estimates using the dependence case are only about a factor of 1.5 higher than those using the independence case).

Five human occupational exposures were simulated: constant exposure to 10, 25, 50, 100 or 500 ppm MC for 8-hrs per day and 5 days per week. Simulations were made up to 4 weeks of work, at which a dynamic equilibrium was reached, and as with mice, were performed using 5000 parameter human vectors drawn from their joint posterior distribution, augmented by allowing for additional variability in human body weight and work intensity (the latter linked to changes in cardiac, ventilation-perfusion and regional blood flow as described above).

g. Sensitivity Analysis. The influence of variability in mouse and human PBPK model parameters on variability in predicted mouse and human GST lung metabolism was assessed by computing pairwise correlation coefficients using each parameter vector (i.e., the marginal posterior distribution) and the corresponding vector of model predictions. For mice, the sensitivity to predicted GST—lung metabolism in the simulated 2000 ppm bioassay dose group was evaluated. For humans, predicted GST—lung metabolism for an occupational exposure to 25 ppm was considered. Pairwise correlation coefficients were computed using 5000 parameter vectors drawn from the joint posterior distribution and the associated model output vector.

Table VI–6 presents the results from the sensitivity analysis. The strongest pairwise correlation between predicted lung GST metabolism and any input parameter, for either mouse or human simulations, was A2. For the mouse simulation of a 2000 ppm exposure, B2 gave the next strongest pairwise correlation. The mouse parameters QlivC, VlivC, VmaxC, Pfat and QppC all exhibited more moderate (though not negligible) correlations. For the human occupational simulation, the parameters KfC, VmaxC, Sp__Kf, and B2 all exhibited moderate pairwise correlations with human lung GST metabolism. For both mice and human sensitivity analyses, there were a half-dozen or more parameters exhibiting weak (r between 0.1 and 0.2) correlations. It is important to note that all parameters are further correlated via their posterior joint distribution function. This explains why the sum of the regression coefficients (i.e., squares of the correlation coefficients) is greater than 1. Thus considerable care should be exercised in quantitatively estimating the ability of variability in any input parameter to explain variability in predicted GST metabolism, especially among parameters with similar pairwise correlation coefficients.

TABLE VI–6.—CORRELATION COEFFICIENTS FOR TOTAL GST LUNG METABOLISM FROM MONTE CARLO ANALYSIS USING MOUSE AND HUMAN POSTERIOR DISTRIBUTIONS

Mouse 2000 PPM		Human 25 PPM	
Parameter	Correlation coefficient (r)	Parameter	Correlation coefficient (r)
A2	0.860	A2	0.850
B2	0.530	KfC	0.315
QliC	0.335	VmaxC	−0.291
VliC	−0.248	Sp—Kf	0.232
VmaxC	−0.229	B2	0.221
Pfat	−0.203	Pmar	−0.183
QppC	−0.202	QfatC	0.180
VPR	0.193	B1	0.179
Pli	−0.173	VliC	0.161
A1	−0.149	VmarC	0.146
QgiC	−0.145	Work	0.142
Pmar	0.144	QwpC	0.141
VwpC	−0.121	VfatC	0.136
KfC	0.120	QmarC	0.136
Pwp	−0.106	Km	−0.095
VluC	−0.120	QC	−0.083
B1	−0.093	QliC	−0.083
QmarC	−0.083	A1	−0.071
Ppp	−0.076	QgiC	−0.065
VgiC	0.074	Pfat	−0.061
Pgi	0.054	Pwp	−0.058
QC	−0.049	VluC	−0.052
BW	−0.042	Pgi	−0.050
Plu	0.039	VwpC	0.041
Km	−0.035	Pblood	0.039
tVmaxC	0.024	dVPR/dW	0.039
QfatC	0.020	BW	−0.038
Pblood	0.019	dQli/dW	−0.033
VfatC	−0.013	Plu	0.023
Vmar	−0.007	Ppp	0.021
		dQfat/dW	0.016
		VgiC	−0.012
		Pli	−0.010
		dQgi/dW	−0.010
		dQmar/dW	−0.009
		VPR	0.006
		dQC/dW	−0.000
		dQwp/dW	−0.000

h. Posterior PBPK Parameter Distributions. Table VI–7 lists the posterior distributions for mouse PBPK parameters obtained by Bayesian updating of the prior distributions using the available gas uptake data. Comparison of the prior and posterior probability distributions reveals that the gas uptake data retain considerable influence on the distributions of many of the important PBPK model parameters. Medians of the posterior distributions for VPR, Qfat, Pblood, Pmar, Km, A1, and A2 were all appreciably different than the medians for their corresponding prior distributions. Percent CVs for nearly all posterior distributions were considerably smaller than those of their prior distributions. As expected, the marginal variances for the metabolic constants were considerably greater than what was obtained under nonlinear maximum likelihood regression analysis with all other model parameters fixed at nominal values.

TABLE VI–7. PRIOR AND POSTERIOR (FITTED) DISTRIBUTIONS OF THE MOUSE MODEL PARAMETERS

	Parameter	Central tendency		Maximum posterior	Variability	
		Prior median	Posterior median		Prior %CV	Posterior %CV
Flows:						
QCC	Cardiac Output (l/hr/kg__BW)	34.8	34.4	37.6	18	9
VPR	Alveolar Ventilation Perfusion Ratio	1.22	1.59	1.49	75	14
Tissue Blood Flows (fraction of cardiac output):						
QgiC	GI Tract	0.165	0.140	0.175	26	16

TABLE VI–7. PRIOR AND POSTERIOR (FITTED) DISTRIBUTIONS OF THE MOUSE MODEL PARAMETERS—Continued

	Parameter	Central tendency		Maximum posterior	Variability	
		Prior median	Posterior median		Prior %CV	Posterior %CV
QliC	Liver	0.017	0.020	0.017	19	16
QfatC	Fat	0.047	0.090	0.098	43	19
QppC	Poorly Perfused Tissues	0.276	0.290	0.243	22	18
QwpC	Well Perfused Tissues	0.369	a 0.360	0.378		a
QmarC	Bone Marrow	0.089	0.100	0.090	51	27
Tissue Volumes (fraction of body weight):						
VgiC	GI Tract	0.035	0.040	0.038	26	22
VliC	Liver	0.045	0.050	0.050	18	12
VfatC	Fat	0.077	0.070	0.055	35	24
VppC	Poorly Perfused Tissues	0.556	b 0.540	0.569		b
VwpC	Well Perfused Tissues	0.065	0.070	0.065	14	12
VluC	Lung	0.008	0.010	0.007	27	22
VmarC	Bone Marrow	0.033	0.040	0.037	42	29
Equilibrium Partition Coefficients:						
Pblo	Blood:Air	13.7	18.5	13.1	66	18
Pgi	GI Tract:Air	10.5	11.3	9.5	19	17
Pli	Liver:Air	22.9	28.2	23.9	79	32
Pfat	Fat:Air	98.2	100.5	106.7	35	21
Ppp	Poorly Perfused Tissues:Air	9.5	12.1	13.1	27	17
Pwp	Well Perfused Tissues:Air	10.2	10.4	10.3	19	16
Plu	Lung:Air	10.0	11.3	12.5	27	22
Pmar	Bone Marrow:Ait	62.0	70.4	89.2	50	25
Metabolic Parameters:						
VmaxC	Maximum metabolic velocity of MFO saturable pathway (mg/hr/kg__liver).	750	718	661	1413	12
tVmaxC	Maximum metabolic velocity of MFO saturable pathway in t-DCE pretreated mice.	8.4	7.2	11.3	58	50
Km	Affinity of MFO saturable pathway (mg/l)	1.35	0.04	0.03	1413	97
KfC	First order rate constant for GST pathway (l/hr/kg^0.25).	1.5	1.77	2.47	1413	24
A1	Ratio of lung to liver in-vitro MFO metabolic velocities (nmol/min/gm__lung__micros.Prot)/(nmol/min/gm__liver__micros.Prot).	0.405	0.28	0.30	54	31
A2	Ratio of lung to liver in-vitro GST metabolic velocities (nmol/min/gm__lung__cytos.Prot)/(nmol/min/gm__liver__cytos.Prot).	0.282	0.37	0.30	55	41
B1	Ratio of lung and liver tissue content of microsomal protein.	0.271	0.26	0.29	23	18
B2	Ratio of lung and liver tissue content of cytosolic protein.	0.721	0.70	0.84	22	17

Notes: (a) functionally defined as 1__sum (other fractional flows); (b) functionally defined as 0.82__sum (other fractional volumes).

Table VI–8 presents the corresponding set of results for human PBPK parameters. The human *in vivo* data also appeared to contain considerable information about many of the model parameters, as evidenced by shifts in medians and tightening of posterior distributions relative to priors. Fitted estimates of the metabolic constants were fairly precise, even for Km (Table VI–8); indeed, the fits were markedly superior to those shown in Andersen et al. [Ex. 21–94] and Clewell et al. [Ex. 96].

TABLE VI–8.—Prior and Posterior (Fitted) Distributions of the Human Model Parameters

	Parameter	Prior distribution			Posterior distribution			
		GM	GSD	%CV	Posteriors for Bayesian fit		Modified by exercise	
					Median	%CV	Median	%CV
Flows:								
QCC	Cardiac Ouput (1/hr/kg__BW).	4.2	1.10	10	4.0	6	6.2	17

TABLE VI–8.—Prior and Posterior (Fitted) Distributions of the Human Model Parameters—Continued

	Parameter	Prior distribution			Posterior distribution			
		GM	GSD	%CV	Posteriors for Bayesian fit		Modified by exercise	
					Median	%CV	Median	%CV
VPR	Alveolar Ventilation Perfusion Ratio.	1.35	1.15	15	1.03	1	1.37	9
Tissue Blood Flows (fraction of cardiac output):	.....	.....	.....	.....	.....	.....	.....	.....
QgiC	GI Tract	0.191	1.25	23	0.149	12	0.122	14
QliC	Liver	0.067	1.20	19	0.063	15	0.041	24
QfatC	Fat	.057	1.45	38	0.045	10	0.052	11
QppC	Poorly Perfused Tissues.	0.198	1.55	a	0.378	a 9	a 0.453	10
Qwpc	Well Perfused Tissues.	0.443	1.25	23	0.294	3	0.258	7
QmarC	Bone Marrow	0.044	1.70	57	0.071	38	0.072	38
Tissue Volumes (fraction of body weight):	.....	.....	.....	.....	.....	.....	.....	.....
VgiC	GI Tract	0.017	1.10	10	0.018	8	0.018	8
VliC	Liver	0.026	1.10	10	0.026	8	0.026	8
VfatC	Fat	0.204	1.20	18	0.183	11	0.183	11
VppC	Poorly Perfused Tissues.	0.470	1.15	b	0.489	b 5	b 0.489	5
VwpC	Well Perfused Tissues.	0.044	1.10	9	0.47	7	0.047	7
VluC	Lung	0.008	1.15	14	0.008	11	0.008	11
VmarC	Bone Marrow	0.050	1.10	10	0.049	8	0.049	8
Equilibrium Partition Coefficients:	.....	.....	.....	.....	.....	.....	.....	.....
PC.blood	Blood:Air	8.4	1.30	26	16.5	2	16.5	2
PC.gi	GI Tract:Air	8.1	1.60	50	10.7	36	10.7	36
PC.li	Liver:Air	9.9	1.60	50	13.7	33	13.7	33
PC.fat	Fat:Air	97.6	1.25	22	84.4	12	84.4	12
PC.pp	Poorly Perfuse Tissue:Air.	6.8	1.60	48	13.3	13	13.3	13
PC.wp	Well Perfused Tissue:Air.	7.6	1.40	35	13.1	14	13.1	14
PC.lu	Lung:Air	7.6	1.50	43	9.4	33	9.4	33
PC.mar	Bone Marrow:Air	48.8	1.60	49	47.8	27	47.8	27
Metabolic Parameters:	.....	.....	.....	.....	.....	.....	.....	.....
VmaxC	Maximum MFO metabolic rate (mg/mg/hr/kg_liver).	75.0	10.00	1413	97.2	11	97.2	11
Km	MFO Michaelis Menton constant (mg/1).	0.60	10.00	1413	0.52	39	0.52	39
Kf	1st order rate constant for GST pathway (1/hr).	0.12	2.07	81	0.23	63	0.23	63
A1	[V/S]_lung/[V/S_MFO_liver.	0.0045	4.50	226	0.024	77	0.024	77
A2	[V/S]_lung/[V/S]_GST_liver.	0.236	2.04	83	0.364	49	0.364	49
B1	[mg micr.Prot/gm lung]/[mg micr.Prot/gm liver].	0.297	1.10	10	0.300	8	0.300	8
B2	[mg cyt. Prot/gm lung]/[mg cyt.Prot/gm liver].	0.807	1.20	18	0.845	15	0.845	15

Notes (a) operationally defined as 1—sum (other fractional flows); (b) functionally defined as 0.82—sum (other fractional volumes).

Tables VI–9 and VI–10 compare the posterior distributions for mice and human PBPK parameters with the distributions used by Clewell. For mice, there were appreciable differences in the median values for QCC, VPR, QfatC, QwpC, VwpC, VmaxC, Km, KfC, and the apparent A1 (i.e., A1 × B1). With the exception of VliC, Pblood, Pliv, Ppp and Km, the posterior distributions for all other parameters were tighter than the distributions used by Clewell. The human posterior distributions in Table VI–10 are somewhat different than those in Table VI–8, in that they reflect the influence of modeling variable work intensity on QC, VPR, and all regional blood flows. In comparing these modified posterior distributions to the distributions used by Clewell, one finds appreciable differences in median values for VPR, many of the fractional blood flows (QgiC, QliC, QppC, QwpC), VgiC, PCblood, PCliv, PCfat, VmaxC, KfC, and the apparent A2 (i.e., A2 × B2). All human posterior distributions except for VliC, Pli, and Sp__Kf, had appreciably tighter distributions than those used by Clewell et al. [Ex. 96].

TABLE VI–9.—COMPARISON OF MOUSE PROBABILITY DISTRIBUTIONS USED BY CLEWELL ET AL. WITH OSHA'S POSTERIOR PROBABILITY DISTRIBUTIONS

	Parameter	Central tendency		Variability	
		Clewell et al. median	OSHA median	Clewell et al. %CV	OSHA %CV
Flows:					
QCC	Cardiac Output (1/hr/kg__BW)	[a] 41.5	34.4	9	9
VPR	Alveolar Ventilation Perfusion Ratio	[b] 1.76	1.59	58	14
Tissue Blood Flows (fraction of cardiac output):					
QgiC	GI Tract	0.165	0.14	25	16
QliC	Liver	0.035	0.02	96	16
QfatC	Fat	0.030	0.09	60	19
QppC	Poorly Perfused Tissues	0.250	0.29	40	18
QwpC	Well Perfused Tissues	0.520	c 0.36	50	c
QmarC	Bone Marrow	NA	0.10	NA	27
Tissue Volumes (fraction of body weight):					
VgiC	GI Tract	0.031	0.04	30	22
VliC	Liver	0.046	0.05	6	12
VfatC	Fat	0.100	0.07	30	24
VppC	Poorly Perfused Tissues	0.513	d 0.54	30	d
VwpC	Well Perfused Tissues	0.041	0.07	30	12
VluC	Lung	0.008	0.01	30	22
VmarC	Bone Marrow	NA	0.04	NA	29
Equilibrium Partition Coefficients:					
Pblo	Blood:Air	23.0	18.5	15	18
Pgi	GI Tract:Air	11.4	11.3	30	17
Pli	Liver:Air	38.7	28.2	20	32
Pfat	Fat:Air	107.0	100.5	30	21
Ppp	Poorly Perfused Tissues:Air	8.5	12.1	10	17
Pwp	Well Perfused Tissues:Air	11.4	10.4	20	16
Plu	Lung:Air	10.0	11.3	30	22
Pmar	Bone Marrow:Air	NA	70.4	NA	25
Metabolic Parameters:					
VmaxC	Maximum metabolic velocity of MFO saturable pathway (mg/hr/kg__liver).	970	718	20	12
Km	Affinity of MFO saturable pathway (mg/l)	1.35	0.04	30	97
KfC	First order rate constant for GST pathway (l/hr/kg__0.25)	1.5	1.77	30	24
A1	Ratio of lung to liver in-vitor MFO metabolic velocities (nmol/min/gm__lung__micros.Prot)/(nmol/min/gm__liver__micros.Prot).	0.405	0.28	50	31
A2	Ratio of lung to liver in-vitro GST metabolic velocities (nmol/min/gm__lung__cytos.Prot)/(nmol/min/gm__liver__cytos.Prot).	0.282	0.37	50	41
B1	Ratio of lung and liver tissue content of microsomal protein	1	0.25	0	18
B2	Ratio of lung and liver tissue content of cytosolic protein	1	0.69	0	17

Notes: (a) value computed for 0.025 kg mouse; (b) unitless; (c) functionally defined as 1—sum (other fractional flows); (d) functionally defined as 0.82—sum(other fractional volumes); (na) not applicable.

TABLE VI–10. COMPARISON OF HUMAN PROBABILITY DISTRIBUTIONS USED BY CLEWELL ET AL. WITH OSHA'S POSTERIOR PROBABILITY DISTRIBUTIONS

	Parameter	Central tendency		Variability	
		Clewell et al. median	OSHA median	Clewell et al. %CV	OSHA %CV
Flows:					

TABLE VI–10. COMPARISON OF HUMAN PROBABILITY DISTRIBUTIONS USED BY CLEWELL ET AL. WITH OSHA'S POSTERIOR PROBABILITY DISTRIBUTIONS—Continued

	Parameter	Central tendency		Variability	
		Clewell et al. median	OSHA median	Clewell et al. %CV	OSHA %CV
QCC	Cardiac Output (l/hr/kg__BW)	[a] 6.2	[c] 6.3	9	[c] 17
VPR	Alveolar Ventilation Perfusion Ratio	[b] 1.95	[c] 1.36	18	[c] 9
Tissue Blood Flows (fraction of cardiac output):					
QgiC	GI Tract	0.195	[c] 0.12	10	[c] 13
QliC	Liver	0.070	[c] 0.04	35	[c] 23
QfatC	Fat	0.050	[c] 0.05	30	[c] 15
QppC	Poorly Perfused Tissues	0.240	[c] 0.46	15	[c] 10
QwpC	Well Perfused Tissues	0.445	[c, d] 0.26	20	[c, d] 7
QmarC	Bone Marrow	NA	[c] 0.07	NA	[c] 45
Tissue Volumes (fraction of body weight):					
VgiC	GI Tract	0.045	0.017	10	8
VliC	Liver	0.023	0.026	5	8
VfatC	Fat	0.160	0.187	30	12
VppC	Poorly Perfused Tissues	0.480	[e] 0.483	30	[e] 5
VwpC	Well Perfused Tissues	0.033	0.047	10	7
VluC	Lung	0.006	0.008	10	12
VmarC	Bone Marrow	NA	0.050	NA	8
Equilibrium Partition Coefficients:					
Pblo	Blood:Air	12.9	16.5	15	2
Pgi	GI Tract:Air	12.0	13.5	30	31
Pli	Liver:Air	37.4	13.6	20	34
Pfat	Fat:Air	117.0	81.2	30	13
Ppp	Poorly Perfused Tissues:Air	10.0	13.3	10	14
Pwp	Well Perfused Tissues:Air	12.0	13.0	20	14
Plu	Lung:Air	10.6	9.1	30	32
Pmar	Bone Marrow:Air	NA	51.2	NA	35
Metabolic Parameters:					
VmaxC	Maximum metabolic velocity of MFO saturable pathway (mg/hr/kg__liver).	75.2	94.2	30	12
Km	Affinity of MFO saturable pathway (mg/l)	0.4	0.49	50	35
KfC	First order rate constant for GST pathway (l/hr/kg − 0.25)	1.5	1.82	50	24
A1	Ratio of lung to liver in-vitro MFO metabolic velocities (nmol/min/gm__lung__micros. Prot)/(nmol/min/gm__liver__micros.Prot).	0.015	0.03	70	69
A2	Ratio of lung to liver in-vitro GST metabolic velocities (nmol/min/gm__lung__cytos.Prot)/ (nmol/min/gm__liver__cytos.Prot).	0.18	0.45	70	71
B1	Ratio of lung and liver tissue content of microsomal protein	1.0	0.31	0	8
B2	Ratio of lung and liver tissue content of cytosolic protein	1.0	0.84	0	14
Sp__Kf	Allometric scaling power for body weight scaling of KFC from mice to humans.	− 0.25	− 0.267	0	22

Notes: (a) value computed for 70 kg human; (b) unitless; (c) posterior distributions adjusted for effects of light activity; (d) functionally defined as 1—sum(other fractional flows); (d) functionally defined as 0.82—sum(other fractional volumes); (NA) not applicable.

i. Alternative analysis using the ''parallelogram'' approach. Andersen et al. [Ex. 21–94] estimated a human first order rate constant (Kf) for glutathione (GST) metabolism of MC in the liver by allometric scaling of a fitted estimate of an *in vivo* mouse rate constant (KfC_{mouse}). Specifically,

$$Kf_{human} = KfC_{mouse} \text{ X } BW^{spKf}$$

where spKf was the allometric scaling power with value − 0.25. In their Monte Carlo analysis, Clewell et al. followed the approach of Andersen et al., treating KfC_{mouse} as a lognormally distributed random variable and spKf as a known constant. The Bayesian analysis summarized above also made use of the allometric scaling given by the equation above, but prior probability distributions were specified for both KfC_{mouse} and spKf.

Reitz et al. (1988, 1989) [Exs. 7–225 and 21–53] proposed an alternative approach for estimating an apparent *in vivo* human Kf. The approach, referred to as the ''parallelogram method,'' assumes there is a constant proportionality across species between *in vitro* and apparent *in vivo* metabolic rates when normalized for substrate concentration ([S]). For example, the equation modeling the apparent *in vivo* rate of GSH conjugation (dM_{GST}/dt) is given by:

$$\frac{dM_{GST}}{dt} = Kf \times [S] \times Vol_{liver}$$

The constant proportionality between apparent *in vivo* rates of metabolism and *in vitro* rates implies

$$\frac{dM_{GST}/dt}{[S]} = k_p \times [V/S]_{GST} = Kf \times Vol_{liver}$$

where $[V/S]_{GST}$ denotes an *in vitro* enzymatic rate normalized to [S] and k_p the *in vivo—in vitro* proportionality constant. This approach assumes a common value of k_p across species, such that knowledge of a $[V/S]_{GST\text{-}rodent}$ and Kf_{rodent} (sufficient to estimate a value for k_p as the ratio of Kf_{rodent} to $[V/S]_{GST\text{-}rodent}$) and knowledge of $[V/S]_{GST\text{-}human}$ is sufficient to estimate the remaining corner of a parallelogram, namely Kf_{human}. Therefore, this approach assumes,

$$\frac{[V/S]_{GST_{human}}}{[V/S]_{GST_{rodent}}} = \frac{Kf_{human}}{Kf_{rodent}}$$

or:

$$Kf_{human} = [V/S]_{GST_{human}} \times \frac{Kf_{rodent}}{[V/S]_{GST_{rodent}}}$$

Reitz et al. [Ex. 21–53] obtained an estimate for Kf_{human} using the parallelogram method that was very similar to the estimate obtained by Andersen et al. [Ex. 21–94] using allometric scaling. However, Reitz and coworkers estimated a mean $[V/S]_{GST\text{-}human}$ based on liver samples from only four human subjects—three of which had appreciable enzymatic activity and one with no detectable activity. More recent publications (Bogaards et al., 1993 [Ex. 127–16]; Graves et al., 1995 [Ex. 122]) and unpublished data (Green et al., 1987 [Ex. 14]) provide measured values of $[V/S]_{GST}$ on another 35 human subjects. These additional data demonstrate considerable variation in rates of GST metabolism among human subjects, consistent with a known human polymorphism for GST, described earlier in this Quantitative Risk Assessment. Moreover, these data indicated that, putting aside questions of interlaboratory comparability of measurements, three of the four human samples used by Reitz et al. had GST metabolic rates among the highest reported to date. Consequently, the mean $[V/S]_{GST\text{-}human}$ used by Reitz and coworkers was *greater* than the mean estimable from the full complement of data on human GST activity.

Since OSHA was interested in assessing the effect of accounting for the full complement of data on human GST activity on estimates of cancer risk, this additional analysis was performed, despite the Agency's reservations concerning the appropriateness of using the parallelogram approach in the MC risk assessment. Although this approach allows the use of all of the available data, the uncertainties in the ratio of *in vitro* to *in vivo* metabolic constants raise serious questions for the utility of this analysis. OSHA is presenting this analysis for purposes of comparison and notes that HSIA and Clewell used allometric adjustments in their final PBPK models.

The use of a Kf_{human} derived by the parallelogram method required: (1) modification of the human PBPK model; (2) specification of a prior probability distribution for Kf_{human}; (3) replication of the Bayesian analysis of the human *in vivo* open chamber data using the new prior for Kf_{human}; (4) simulation of the occupational exposure scenario using the joint posterior distributions from the new Bayesian analysis to obtain a posterior distribution for human GST lung metabolism; and (5) re-estimation of the extra cancer risk.

(*1*) *PBPK Model Modifications.* The only structural modification to the PBPK models was to replace the parameter for allometric scaling of Kf_{mouse} with a direct insert of a model parameter Kf_{human}, having its own prior probability distribution.

(*2*) *Prior Probability Distributions.* Mouse prior probability distributions were unchanged. Prior probability distributions for human model parameters were also unchanged, with the exception of prior distributions for KfC, spKf and A2. Prior probability distributions for KfC and spKf were replaced with a prior probability distribution for Kf_{human}. The prior probability distribution for A2 was modified to account for additional data on human lung GST activity submitted to OSHA by HSIA [Ex. 122].

The prior probability distribution for Kf_{human} was derived using the equation:

$$Kf_{human} = Kf_{rodent} \times \frac{[V/S]_{GST_{human}}}{[V/S]_{GST_{rodent}}} \times err_{k_p}$$

where err_{kp} is an error term added to account for uncertainty in estimating the proportionality constant k_p, as k_{mouse}. Thus, to derive a prior probability distribution for Kf_{human}, it was necessary to derive prior distributions for Kf_{rodent}, $[V/S]_{GST\text{-}rodent}$, $[V/S]_{GST\text{-}human}$ and err_{kp}, which in turn were propagated using Monte Carlo techniques in accordance with the relationships specified by the equation above.

(*i*) *Prior distribution for rodent Kf.* The posterior probability distribution used in the main analysis for the apparent *in vivo* rodent KfC parameter was used as the basis for a prior probability distribution for Kf_{rodent}. The posterior distribution was well described by a truncated lognormal distribution with a mean and standard deviation of 1.8 and 0.43 l/hr/bw /$^{-0.25}$, and lower and upper truncations at 0.84 and 3.07 l/hr/bw /$^{-0.25}$, respectively. The posterior distribution was converted to units of (hour)$^{-1}$ by using Monte Carlo techniques to multiply the truncated lognormal by the scalar, (rodent body weight)$^{-0.25}$.

(*ii*) *Prior for rodent liver GST [V/S].* A prior probability distribution for a low dose mouse $[V/S]_{GST}$ was obtained as the ratio of the fitted estimates of *in vitro* V_{max} and K_m reported by Reitz et al. for liver glutathione conjugation of MC. The fitted estimates of V_{max} and K_m and their associated standard errors were used to set the parameters for normal distributions. Monte Carlo techniques were used to obtain the ratio of these two distributions (i.e., V_{max}/K_m), under the assumption that the joint sample space for V_{max} and K_m was correlated with a $\pi = 0.9$. Correlation was induced because a reanalysis of the mouse *in vitro* reported in Reitz et al. showed that the joint parameter space for these two fitted parameters was highly correlated.

(*iii*) *Prior distribution for human GST [V/S].* There were four data sets reporting measured values of *in vitro* GST activity in liver samples from 39 human subjects. These data reflect work from different laboratories using (in some cases) different assay methods and different substrate concentrations. In order to make use of all the data to estimate central tendencies and population variability, it was necessary that all measurements be placed on a common scale.

With respect to assay methods, two of the studies [Exs. 21–53 and 122] reported measured values of $[V/S]_{GST}$ based on detection of [36]Cl from labelled MC. The other two studies [Exs. 14 and 127–16] reported values of $[V/S]_{GST}$ based on detection of formaldehyde, a known decomposition product from GSH conjugation with MC. In a comparison of these two methods, Green et al. [Ex. 14] reported results indicating a systematic difference in measured values of $[V/S]_{GST}$, with the [36]Cl detection method appearing to give estimates approximately 1.7-fold higher than the formaldehyde detection method. In this analysis, the [36]Cl method was chosen as the common scale, since the mouse $[V/S]_{GST}$ data used above were based on this method. Thus, the formaldehyde assay results were multiplied by 1.7 to put them on the [36]Cl scale.

Adjustments for both substrate concentration and nonlinear metabolism were made by converting all the

reported *in vitro* velocity data, $[V]_{GST}$, to V_{max}/K_m ratios (i.e., low dose metabolic velocity), by the equation:

$$\frac{V_{max}}{K_m} = \frac{([V]_{GST} \times (K_m + [S]))/[S]}{K_m}$$

The above equation follows from assuming *in vitro* kinetics can be reasonably modeled as a single-substrate Michaelis-Menton process (i.e., $[V]_{GST} = \{V_{max} \text{ x } [S]\}/\{K_m + [S]\}$). In making adjustments, assay specific substrate concentrations were used (i.e., [S], which ranged from 35 to 94 mM) along with the average estimate of an *in vitro* Km reported by Reitz et al. [Ex. 21–53] in analysis of data from two human subjects (44 mM). It is noteworthy that none of the human *in vitro* $[V/S]_{gst}$ data reported in Reitz et al. were truly reflective of linear kinetics, whereas the mice data were.

After the two above adjustments were made, a lognormal distribution was fit to the transformed data yielding a GM of 0.031 l/min/mg protein, and a GSD of 2.72. This distribution models intersubject variability in in vitro metabolic activity. However, the prior probability distribution for $[V/S]_{gst\text{-}human}$ should reflect variation in means of six subjects, because the *in vivo* human data from Dow Chemical Company reflect the averaged pharmacokinetic behavior of tissue from six subjects. Thus, dispersion in the above distribution was adjusted to give the corresponding sampling distribution for means of n = 6.

(iv) Prior distribution for error term.

The *in vivo* and *in vitro* metabolic data on the MFO metabolic pathway, reported by Reitz et al. [Ex. 21–53], were used to estimate the uncertainty in assuming a constant k_p across species. These were the only data for which both in vivo and *in vitro* information was available on several species and which was directly relevant to MC. To avoid artifacts due to the very imprecise fitted estimates of apparent *in vivo* Km's, *in vivo* / *in vitro* comparisons were constructed based on estimates of Vmax alone. These estimates were then normalized by the ratio obtained for mice, providing a measure of the error in using a mouse ratio to estimate ratios in three other species: rats (1.42), hamsters (0.64), and humans (0.41). The GM (0.72) and GSD (1.89) of these three values were used to set parameters for a lognormal distribution used as the prior probability distribution for err_{kp}. Note that the human value of 0.41 reflected an average of separate estimates on four human subjects, with ratios ranging from 0.1 to 1.0.

(v) Monte Carlo simulation to obtain a prior for human Kf. The above prior probability distributions for Kf_{mouse}, $[V/S]_{gst\text{-}mouse}$, $[V/S]_{GST}$ and err_{kp} were independently sampled by Monte Carlo techniques (n = 5000) and combined to give a prior distribution for Kf_{human} for use in Bayesian analysis of the human open chamber data.

(vi) Revised prior distribution for A2.

A2 is the ratio of *in vitro* GST enzymatic activity in lung tissue to the same activity in liver tissue. In the main analysis, the prior probability distribution for A2 was derived according to the equation:

$$A2 = \frac{[V/S]_{GST_{lung}}}{[V/S]_{GST_{liver}}} \times err_{vivo/vitro}$$

where $err_{vivo/vitro}$ is an error term to account for uncertainty in using a ratio of *in vitro* activity to make inferences about in vivo activity, and the data of Reitz et al. [Ex. 21–53] were used to estimate prior distributions for $[V/S]_{GST\text{-}lung}$ and $[V/S]_{GST\text{-}liver}$. This prior distribution was revised to account for additional human $[V/S]_{GST\text{-}lung}$ and $[V/S]_{GST\text{-}liver}$ data.

(vii) Prior for human lung GST [V/S]. Previously, only a single measured value for $[V]_{GST\text{-}lung}$ from a pooled lung sample from two human subjects was available for estimating A2. Mainwaring et al. [Ex. 124] recently submitted additional $[V]_{GST\text{-}lung}$ data to OSHA, consisting of measured values on three additional human subjects (0.00, 0.06 and 0.21 nmol/min/mg protein). The value reported as 0.00 was assumed equal to one-half the detection limit for the assay. Since these new $[V]_{GST\text{-}lung}$ data were obtained using the formaldehyde detection assay, it was necessary to transform the values to the [36]Cl scale. Lacking direct information, it was assumed that the same HCOOH ‰ [36]Cl correction factor derived for the liver data held for the lung data. A correction for substrate concentration was also made, under the assumption of equivalency in lung and liver *in vitro* Km's. The resulting transformed $[V]_{GST\text{-}lung}$ data were used to construct a prior probability distribution describing uncertainty in the mean of five [1] observations (GM = 0.00082, GSD = 1.61). Note that, in this case, an attempt was made to model pure uncertainty in a low dose $[V/S]_{GST\text{-}lung}$, without information indicating appreciable heterogeneity in the ratio of lung and liver enzymatic activity within an individual.

(viii) Prior probability distribution for uncertainty in human liver GST [V/S]. Because of the focus on uncertainty in A2, the prior probability distribution for $[V/S]_{GST\text{-}liver}$ derived above was modified to describe uncertainty about the mean, given a sample size of 39 subjects.

(ix) Uncertainty in using an in vitro ratio of lung and liver GST activity to make an inference about the corresponding ratio for apparent in vivo GST activity. A prior probability distribution for $err_{vivo/vitro}$ was derived using data on *in vivo* and *in vitro* ratios of liver MFO enzymatic activity for different species, as a surrogate for intra-species lung versus liver GST enzymatic activity. Thus, two key assumptions are made: (i) That relative enzymatic activity for liver tissue from two species is a reasonable surrogate for relative activities of lung versus liver tissue within a single species, and (ii) that the degree of consistency in ratios of *in vivo* versus *in vitro* enzymatic activity will be the same for either MFO or GST mediated processes.

If the apparent *in vivo* Vmax for the MFO pathway in the lung was modeled as:

$$V_{max_{MFO_{lung}}} = V_{max_{MFO_{liver}}} \times \frac{[V/S]_{MFO_{lung}}}{[V/S]_{MFO_{liver}}} \times \frac{Vol_{lung}}{Vol_{liver}}$$

it follows that,

$$\frac{V_{max}A_{MFO_{lung}}}{V_{max}A_{MFO_{liver}}} = \frac{[V/S]_{MFO_{lung}}}{[V/S]_{MFO_{liver}}}$$

where VmaxA denotes normalization of Vmax to unit tissue volume. Although there were insufficient data to

[1] Since the single observation of $[V]_{GST\text{-}lung}$ reported by Reitz et al. (1988) was from a pooled sample of lung tissue from two human subjects, the data point was treated as two observations with the same value.

allow for a direct evaluation of the above equation, the data tabulated by Reitz et al. [Ex. 7–225] for MFO enzymatic activity in mice, rats and hamsters did allow an evaluation of the equality,

$$\frac{V_{max}A_{MFO_{liver_{sp1}}}}{V_{max}A_{MFO_{liver_{sp2}}}} = \frac{[V/S]_{MFO_{liver_{sp1}}}}{[V/S]_{MFO_{liver_{sp2}}}}$$

where the subscripts sp1 and sp2 denote species 1 and 2 (e.g., mouse and rat). Using the apparent in vivo Vmax and *in vitro* [V/S] data reported in Reitz et al. [Exs. 7–225 and 21–53], it was possible to compute mouse:rat, hamster:mouse and rat:hamster ratios for in vivo Vmax and *in vitro* [V/S] as shown in table VI–11, below.

TABLE VI–11.—Interspecies Comparison of MFO Activity

Species ratio	Ratios of MFO enzymatic activity		
	in vivo Vmax	in vitro [V/S]	Fold-Difference *
Rat: mouse	0.49	0.36	1.36
Mouse: hamster	1.20	0.79	1.53
Hamster: rat	0.59	0.28	2.06

* Ratio of values in *in vivo* Vmax column to values in *in vitro* [V/S] column.

The assumption was made that the use of an *in vitro* ratio as a surrogate for an *in vivo* ratio is unbiased (i.e., $err_{vivo/vitro}$ should be centered on a value of 1). The mean of the three estimates of fold-difference (1.65) is our best estimate of a GSD for $err_{vivo/vitro}$. Thus, the prior probability distribution for $err_{vivo/vitro}$ was modeled as a lognormal variate with expected value 1.0 and GSD of 1.65.

(x) Monte Carlo simulation to obtain a prior probability distribution for A2. The above prior probability distributions for [V/S]GST-lung, [V/S]GST-liver and $err_{vivo/vitro}$ were independently sampled by Monte Carlo techniques (n = 5000) and combined to give a prior probability distribution for A2 for use in Bayesian analysis with the human open chamber data. The resulting distribution was well described as a lognormal variate with a GM of 0.236 and a GSD of 2.0.

(3) Human in vivo data and simulating occupational exposure. Bayesian updating was performed with the same human *in vivo* data used in the main analysis. These data consisted of time serial measurements of exhaled breath and venous blood concentrations of MC for 6 human volunteers exposed to 100 and 350 ppm MC for 6 hours. Unfortunately, the data have only been reported as averages of the 6 subject-specific observations at each time point. When simulating the human data, subjects were assumed to be at rest (i.e., work load set equal to 0), and the reported average body weight for the six subjects (86 kg) was assumed to be known without error.

A single human occupational exposure was simulated: constant exposure to 25 ppm MC for 8-hours per day and 5 days per week.

(4) Distribution of human metabolized dose and sensitivity analysis. The distribution for GST metabolism in the human lung resulting from simulated occupational exposure to 25 ppm MC had a median and mean of 0.139 and 0.192 mg/day/liter lung, about 3-fold less than values obtained using the allometrically scaled Kf.

From the sensitivity analysis, Kf and A2′ exhibited the strongest pairwise correlations with predicted lung GST metabolism, with all other parameters having considerably smaller correlation coefficients. Indeed, other than PC.mar (partition coefficient air:marrow), all other parameters were only weakly correlated with GST lung metabolism. These results differ somewhat from those obtained when using an allometrically scaled Kf, and reflect the effect of greater variability in a Kf based on the parallelogram method.

(5) Posterior distributions in the ''parallelogram method'' analysis. The posterior distributions for many model parameters were considerably tighter than their corresponding prior distributions, most notably for fractional blood flow and partition coefficient parameters. Similar results were obtained in the main analysis. In general, medians and %CVs of the posterior distributions were similar to those in the main analysis, with the exception of Kf, which was expected, given its revised prior distribution. However, differences among the posterior distributions for Kf were less than expected due to an appreciable shift toward larger values (and some tightening) in the posterior distribution for the parallelogram-based Kf relative to its prior distribution. Thus, it would appear that the data had some information about plausible values of Kf.

The results of the covariance analysis indicated that the covariance structure was fairly similar to the results from the main analysis, with moderate to high pairwise correlations among 15 pairs of parameters.

G. Results of OSHA's PBPK Risk Assessments; Discussion

Summary statistics for OSHA's main analysis modifying the other analysis and the alternative (parallelogram) analysis are reported in Table VI–12. From the main analysis, the MLE of excess cancer risk obtained using the upper 95th percentile of the human internal dose distribution was 3.62/1000, for an occupational lifetime exposure to 25 ppm MC. The MLE of cancer risk obtained using the mean of the human internal dose distribution was 1.24/1000. The alternative (parallelogram) analysis yielded slightly lower estimates of risk. In that analysis, the MLE of cancer risk using the upper 95th percentile of the human internal dose distribution was 1.23/1000. The MLE of cancer risk for the alternative analysis using the mean of the human internal dose distribution was 0.40/1000. After evaluating the methodologies and uncertainties in the two analyses, OSHA determined that the main analysis was most appropriate for the Agency's final risk assessment and the MLE of cancer risk using the upper 95th percentile of the human internal dose distribution was best supported as OSHA's final MC risk estimate. Therefore, OSHA's final risk estimate for occupational lifetime exposure to MC at 25 ppm is 3.62/1000.

TABLE VI–12.—Summary Statistics on Estimates of Extra Cancer Risk From Occupational Exposure to 25 ppm MC FOR 8 HRS/DAY, 5 DAYS/WK FOR 45 YEARS

Computational approach	Summary statistics for distributions of extra risk				
	95% **	Mean	%CV *	Skewness	Kurtosis
Maximum likelihood fitting: Dependence case.	3.62 *** per 1000	1.24 per 1000	103	2.2	10.2

TABLE VI–12.—Summary Statistics on Estimates of Extra Cancer Risk From Occupational Exposure to 25 ppm MC FOR 8 HRS/DAY, 5 DAYS/WK FOR 45 YEARS—Continued

Computational approach	Summary statistics for distributions of extra risk				
	95% **	Mean	%CV *	Skewness	Kurtosis
Maximum likelihood fitting: Independence case..	2.43 per 1000	0.79 per 1000	113	2.3	11.3

* %CV denotes coefficient of variation ([standard deviation/mean] x 100).
** 95% denotes the 95th percentile value of the distribution of GST matabolites for extra cancer risk.
*** OSHA's final risk estimate.

Figure VI–1 shows the end result of the main PBPK analysis: the cumulative distribution function of excess lifetime cancer risk ($\log^{10}$ scale) from exposure to 25 ppm MC, 8 hours per day, 5 days per week for 45 years, when estimated using the MLE of the dose-response parameters, GST lung metabolism as the dose surrogate, and a human Kf based on allometric scaling and Bayesian prior information. As described in the main analysis, the ''dependence case'' was used. Several summary statistics can be discerned from this cumulative distribution function: (1) the 95th percentile of this hybrid distribution of uncertainty and heterogeneity gives a risk estimate of 3.62×10^{-3} (point ''A'' in the figure); (2) the mean value of the distribution (point ''B'' in the figure) gives a risk estimate of 1.24×10^{-3}.

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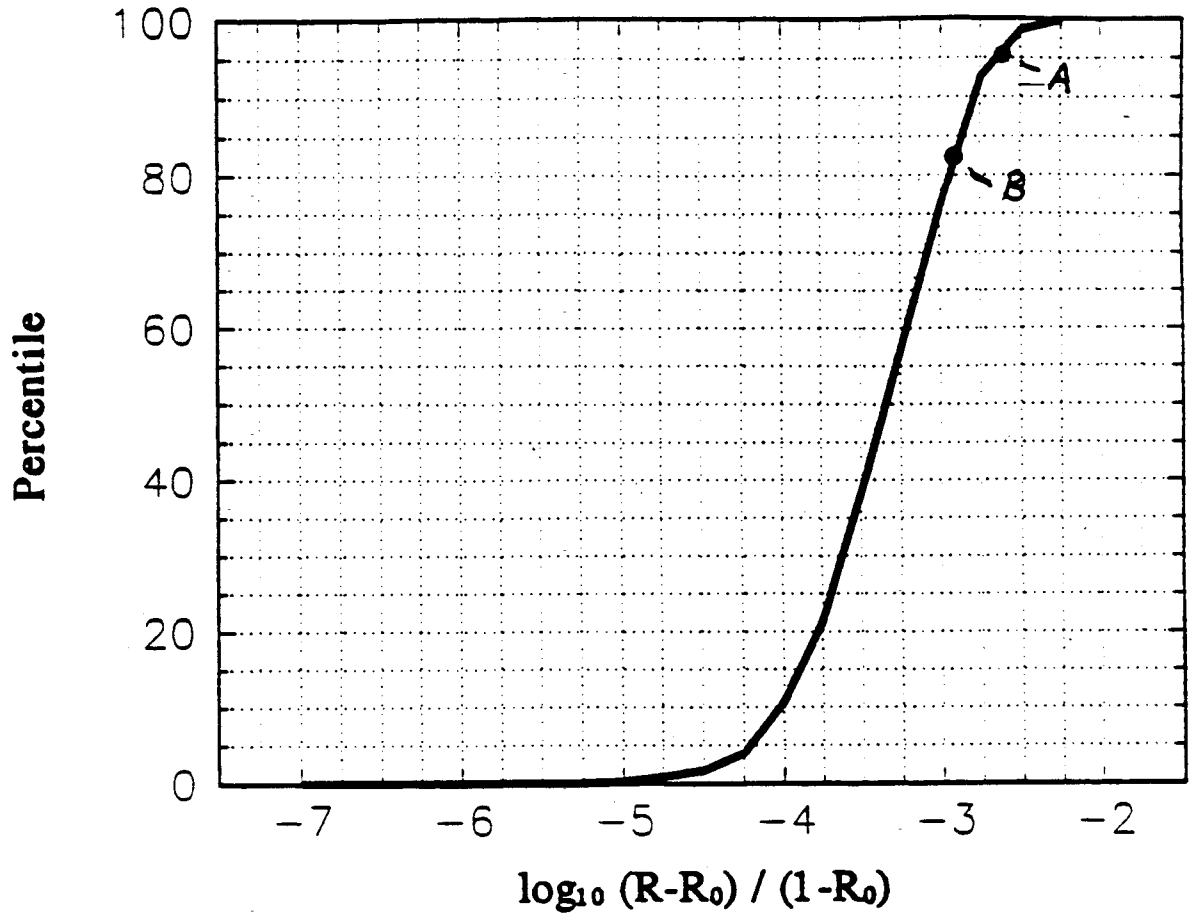

Figure VI-1 *Dependence case*; Estimated cumulative distribution of human cancer risk linked to a 45 year occupational exposure to methylene chloride, at 25 ppm in the air, 8 hours/day, 5 days per year. Generated using the results described in Figure 3.

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OSHA conducted the alternative analysis in order to determine the impact of basing the human GST metabolite distribution on allometry (human GST metabolic rates estimated based on the relative size of animals and humans) versus the parallelogram approach (human GST metabolic rates based on ratio of various rodent *in vitro*: *in vivo* metabolic rates applied to human *in vitro* rates) on risk estimates. As discussed in greater detail above, allometry predicts that one would expect that humans have approximately seven-fold less GST activity than mice. The parallelogram approach, on the other hand, predicts approximately 18-fold less GST activity in humans than in mice. After analyzing the available data, OSHA has determined that the allometric assumptions are best supported by the scientific literature, primarily because of the lack of human *in vivo* GST data and the lack of validation of the parallelogram approach. The Agency has therefore used that approach in its final (main) estimate of risk, but has also presented an alternative analysis using the parallelogram methodology.

During the rulemaking, studies were submitted to the Agency by HSIA challenging the relevance of the mouse data for estimating human cancer risks. However, as described in detail previously, if one examines the HSIA data critically, it is clear that the studies most likely could not detect differences in metabolic activity (and hence in risk) between mice and humans of the magnitude predicted by allometry. For example, the lack of detection of an increase in DNA ss breaks in human cells compared to mouse cells could be explained because the methodology used could not detect an increase in ss breaks 7-fold smaller than that observed in mice. Clearly, an 18-fold difference, as predicted by the parallelogram method, would be even harder to detect.

Moreover, if the human *in vitro* data are examined more closely, it becomes apparent that the *in vitro*: *in vivo* ratios calculated for the 35 individual humans who have been studied were as low as 4.6 (the median value in this series was 24). Therefore, the use of allometry (ratio = 7) or the parallelogram approach (ratio = 18) would lead to risk estimates that clearly underestimate the risks for some individuals. In addition, RNA adduct data [Ex. 126–25] indicate that exposure of human cells to MC results in only a 3-fold lower amount of RNA adducts than formed in mouse cells. This ratio may not be a close surrogate for the GST ratio, but it does heighten concern that both PBPK approaches may be underestimating cancer risks from occupational exposure to MC, because humans may be appreciably less sensitive than mice.

The distribution of risk presented in either the main or the alternative analysis most closely reflects uncertainty about risk for some randomly chosen worker (with respect to work intensity and body weight), chosen among the population of workers with physiologic, anatomic, and metabolic attributes similar to those of the average subject from the Dow human study group. The Dow pharmacokinetic data did not contain individual data on the 6 subjects, so the results obtained and the predictions made are conditioned by the use of averages. This means that the model is truly only applicable to people who physiologically and biochemically resemble the Dow group of six subjects. Although six subjects do not represent a large data base from which to draw a representative PBPK sample, this is much more human data than is usually available to base a risk assessment on. In fact, in OSHA's preliminary quantitative risk assessment, point estimates were used for body weight, breathing rates, etc. to represent the entire working population with a single ''average'' number. Therefore, this sample, although small, represents a significant improvement over the point estimates of human parameter values for PBPK modeling. Although these are the best data available, the small number of individuals upon which the human parameter values are based increases concern that the Agency may be underestimating risks for a significant portion of the working population by relying upon these values and using PBPK modeling to estimate human internal doses. OSHA considered making an ad hoc inflation of the variance of the distributions of human GST enzyme kinetics parameters in order to account for some of this unmeasured heterogeneity (as recommended by the NAS Committee report discussed above), but decided not to make this ''conservative'' choice but instead to rely on the unadjusted analyses.

OSHA has chosen for its final risk estimate to couple one measure of central tendency (the MLE of the dose-response parameters) with a somewhat ''conservative'' measure (the 95th percentile of the distribution of human GST metabolites (internal dose)). Congress and the courts have permitted—indeed, encouraged—OSHA to consider ''conservative'' responses to both uncertainty and human variability. The OSH Act addresses the latter when it refers, for example, to OSHA's responsibility to set standards such that ''no employee shall suffer material impairment of health* * *;'' a standard that only considered risk to the average employee clearly would not be responsive to the statute. Similarly, the 1980 ''Benzene decision'' affirmed that ''the Agency is free to use conservative assumptions in interpreting the data with respect to carcinogens, risking error on the side of over-protection rather than under-protection.''

In past rulemakings, OSHA has frequently estimated carcinogenic potency via the MLE of the multistage model parameters. The Agency has recently received comments, particularly in a public meeting in February 1996 on risk assessment issues surrounding the first phase of its ''PEL Update'' process, critical of the MLE on the grounds that this estimator can be highly unstable with respect to small fluctuations in the observed bioassay response rates. Although OSHA may in the future move to a different estimator, such as the mean value of the likelihood function of the multistage model parameters, such a change would have neglible practical impact in the case of MC. The observed data in the NTP mouse bioassay follow a nearly precisely linear trend, so the MLE, mean and UCL estimates are all very nearly equivalent to each other.

However, OSHA needs to take particular care not to underestimate risk when it departs from a relatively simple methodology (in this case, the assumption that administered dose is the most relevant measure of exposure) in favor of a relatively more complex and computationally- intensive methodology (in this case, that the human lung GST metabolite, calculated via a PBPK model, is the most relevant measure of exposure). This is even more important in this particular PBPK analysis, because the variance of the output distributions represents an unknown hybrid of uncertainty in the various parameters and true heterogeneity among the humans exposed to MC. As Clewell stated with respect to his own PBPK analysis (see discussion above), the 95th percentile estimator provides a modicum of assurance that the risk to the average human—and hence the population risk—is not underestimated.

Moreover, it is critical to use an estimator other than the central tendency here so that it will not be inevitable that the risk to a human of above-average susceptibility (due to enzyme kinetics that produce relatively more reactive metabolite per unit of administered dose, or due to other attributes related to body weight, organ

volumes, partition coefficients, etc.) is not underestimated, potentially by a substantial amount. Any ''conservatism'' introduced by using the 95th percentile of the PBPK output distribution is further attenuated by the unmeasured model uncertainty inherent in this more complex model structure. Several aspects of the model itself are known to be oversimplifications (e.g., assuming the lung is the only tissue at risk); therefore, the resulting risk distributions could be biased downward.

Finally, it is important to note that there is no risk of ''cascading conservatism'' with this 95th percentile estimator; the individual model parameters are permitted to vary over their entire ranges, and the selected percentile is only applied to the distribution resulting from the combined influence of all parameters. Furthermore, the newest refinements to the model ensure that the 95th percentile is not affected by any probability assigned to impossible combinations of parameters. The attention paid to issues of mass balance, covariance structure and truncation ensures that this percentile represents a fully plausible set of input parameters. In sum, the combination of the MLE of the multistage parameters and the 95th percentile of the PBPK output distribution represents a reasonable attempt to account for uncertainty and variability without unduly exacerbating the magnitude or the probability of underestimation of errors.

H. Comparison of Animal-Based Risk Estimates With ''Non-Positive'' Epidemiology Data

Direct comparisons between animal bioassays and human epidemiological studies are difficult to make because experimental protocols between animal and human studies differ substantially. Animals are generally exposed to a fixed dose of a chemical, for several hours per day, from approximately 6–8 weeks of age until study termination, which is usually at 2 years. This would be chronologically equivalent to a human exposure that starts when a human is approximately 4–5 years old and continuing until the human is approximately 74 years old (assuming a 74 year average life-span for humans) [Ex. 89]. This clearly differs from the typical pattern of occupational exposure encountered in epidemiological studies of worker populations. For example, in the Kodak cohort, the workers were never exposed to a constant level of MC; exposure to MC for these workers did not start until their adult life; and most of them were exposed to the chemical for less than one third of their life-span.

Exposure to MC has been found to induce lung and liver cancer in mice and mammary tumors in rats. As discussed above, there are positive epidemiology studies which suggest an association between MC exposure and cancer risk. Because exposure data are inadequate or unavailable, it is not possible to quantify the risks in these studies. OSHA acknowledges that there are also non-positive epidemiology studies.

In 1986, Crump analyzed the preliminary results from the 1964–70 Kodak cohort followed through 1984 and compared them to the rodent bioassay results. The results from the Kodak epidemiological study have also been used by Tollefson et al. [Ex. 7–249], Hearne [Ex. 91–D], and NIOSH to compare the predictions of excess cancer risk from the animal risk assessment models. In addition, Hearne used data from the cellulose triacetate fiber study in Cumberland, Maryland, and a different analytical approach, to validate the excess cancer risk predicted by the animal data [Ex. 91–D]. The details of these analyses can be found in the cited exhibits. OSHA has analyzed the different approaches to assessing the mouse bioassay in light of the epidemiology data and has determined that the approach taken by NIOSH (summarized below) represents the most comprehensive and clearest way to examine those data. OSHA also agrees with the conclusions reached by NIOSH, that the epidemiology results and the mouse bioassay data are not inconsistent with each other.

NIOSH compared the confidence intervals for the standardized mortality ratios (SMRs) from the Kodak study with the predicted confidence intervals derived from OSHA's risk assessment models from the NPRM [Ex. 89]. To estimate predicted SMRs using the multistage model, NIOSH used the following approach:

1. The expected excess number of deaths in each of the exposure groups was derived by multiplying the number of workers in each exposure group by the excess risk as determined by the multistage model (after correcting for dose equivalence between animals and humans, and differences in length of follow-up).

2. This number of expected deaths, derived from the animal data, was then added to the expected (denoted E_p) number of deaths which were derived from the Kodak study, after correcting for the HWE, (this can be viewed as the background risk) to estimate the number of ''observed'' deaths that would have been predicted by the multistage model assuming it was valid for humans (denoted O_p).

3. O_p was then divided by E_p to calculate predicted SMRs and 95% confidence intervals, where calculated.

NIOSH's results indicated that the non-positive findings from the Kodak study were not inconsistent with the predicted risk estimates in OSHA's risk assessment. The predicted confidence intervals from the animal multistage model were completely nested within the observed confidence intervals from the Kodak study. This is not to suggest that results from this non-positive epidemiology study are equivalent to the positive results from the animal inhalation study. Rather, based on these findings, one can conclude that the non-positive results from the Kodak epidemiologic study were not of sufficient power to contradict risk predictions of the multistage model developed from the animal bioassay data (when appropriate adjustments for differences in study protocol were taken into account).

Basically, the Kodak study examined approximately 1000 workers whose average MC exposure was 26 ppm. Therefore, the animal-based potency estimates would predict only about 3 excess cancer deaths in that cohort (the risk at 26 ppm is approximately 3 per 1000), even if they were followed for many decades after exposure ceased. This small predicted excess is clearly too small an increment to be observable with statistical confidence, considering the much larger background of cancer present in the human population. The differences between the NIOSH and Hearne analyses essentially represent different ways to estimate the ''signal-to-noise'' ratio for the Kodak study; OSHA believes that any reasonable method of estimating this ratio would conclude that the Kodak study has insufficient power to rule out a ''signal'' of significant human risk.

NIOSH's approach for adjusting for the healthy worker effect (HWE) was criticized in the comments to the record submitted by Hearne. Hearne stated that the HWE is unlikely to be present in long term cancer studies and therefore an adjustment for the HWE is not necessary [Ex. 91–D]. Hearne argued that since the HWE diminishes with time, the healthy worker effect would have been minimal in the 1946–70 Kodak cohort because the median follow-up period was 32 years and that only 20% of the cohort members were still actively employed [Tr. 10/15/92].

There is evidence in the literature showing that the HWE can be weaker for some types of cancer than for other causes of death; however, in this case NIOSH believed and OSHA agreed that the difference between control and

exposed populations reflected an HWE for cancer. In addition, results from a similar analysis done by NIOSH without the HWE adjustment did not contradict the results including the HWE adjustment. NIOSH testified [Tr. 985–6, 9/21/92] that there would be a difference in the results obtained when adjusting for HWE and the unadjusted results. However, the conclusions reached would not be different. In other words, the analysis still supported the conclusion that the epidemiologic and mouse bioassay results were not inconsistent with each other. OSHA supports NIOSH's position on the use of an adjustment factor for HWE in this cohort. Other criticisms of NIOSH's approach can be found in the hearing transcripts and post-hearing comments. OSHA has evaluated these methodological criticisms and has determined that NIOSH used the best available methodology in analyzing this issue and that their conclusions are supported by those arrived at independently by Crump and by Tollefson et al.

Specifically, NIOSH predicted 23.25 deaths from cancers (at all sites) in the full cohort, after adjusting for the HWE. This value is closer to the observed number (22) than is the unadjusted expected number of deaths (29.61). Looking at lung cancer deaths separately, NIOSH predicted 22.36 deaths for the entire cohort (adjusted for HWE) compared with 22 observed and 28.67 expected by Hearne. Hearne observed no deaths from liver cancer in the entire cohort (1.14 deaths were expected). NIOSH predicted 0.88 deaths from liver cancer when they adjusted for the HWE.

OSHA believes that NIOSH's approach in comparing results from an animal bioassay to those of an epidemiological study is the most reasonable comparison between data sets because it is more accurate and better addresses computational and experimental issues inherent in the data sets. The Agency has evaluated the extent to which the cancer risk calculated using the human data is consistent with the cancer risk calculated using animal data. Based on its review of those studies, OSHA concluded that the human epidemiology results are not inconsistent with the animal bioassays and has determined that the bioassays are the appropriate basis for its quantitative risk assessment.

I. Conclusions

OSHA has determined that MC is a potential occupational carcinogen and has conducted a quantitative risk assessment in order to estimate human risks of cancer after occupational exposure to MC. The Agency reviewed all of the human and animal data on MC and determined that MC is carcinogenic in mice and in rats, causing tumors at multiple sites, in both species, and in both sexes of animals. Some epidemiologic data also indicate an association between MC exposure and excess cancer in exposed workers (statistically significant increases in biliary cancers in textile workers and astrocytic brain cancer in workers exposed to MC in solvent applications). Mechanistic data indicate that MC is likely to be metabolized to a genotoxic carcinogen. MC has been clearly shown to be metabolized by similar enzymatic pathways in rodents and humans, indicating that the metabolic processes which produce cancer in mice and rats are also present in humans. Finally, no data have been presented which demonstrate that the mouse is an inappropriate model for humans because of a physiological or biochemical component or process. Therefore, the Agency has determined that it is appropriate to assess the carcinogenic risks of MC using the NTP mouse bioassay dose-response.

The NTP mouse MC bioassays demonstrated a clear dose-tumor response relationship. OSHA determined that the NTP female mouse lung tumor response was the best data set on which to base a quantitative analysis because there was a clear dose-response, low background tumor incidence and it represented the most sensitive tumor site/sex combination.

After examining the PBPK models submitted to the Agency, OSHA concluded that PBPK modeling estimates of the amount of GST metabolites produced are reasonable dose surrogates for MC and are supported by substantial scientific evidence in the record. For that reason, OSHA has used PBPK modeling in its final risk assessment. OSHA reviewed methodologies used in PBPK models submitted to the Agency and decided to modify and expand an existing model. Specifically, a Bayesian analysis was conducted as described above. Use of the Bayesian model analysis was a logical next step in development and use of pharmacokinetic models for MC. It has great advantages in accounting for the covariance of the PBPK parameters and incorporating distributions of physiological parameters obtained from the scientific literature. OSHA's final estimates of risk use the PBPK analysis described above and are based on the MLE of the dose-response parameters using the upper 95th percentile of the human internal dose distribution. For an occupational lifetime exposure to 25 ppm MC, OSHA estimates an excess risk of 3.6 MC-induced cancer deaths per 1000 workers.

VII. Significance of Risk

A. Introduction.

In the 1980 Benzene decision, the Supreme Court, in its discussion of the level of risk that Congress authorized OSHA to regulate, indicated its view of the boundaries of acceptable and unacceptable risk. The Court stated:

> It is the Agency's responsibility to determine in the first instance what it considers to be a ''significant'' risk. Some risks are plainly acceptable and others are plainly unacceptable. If for example, the odds are one in a billion that a person will die from cancer by taking a drink of chlorinated water, the risk clearly could not be considered significant. On the other hand, if the odds are one in a thousand that regular inhalation of gasoline vapors that are 2 percent benzene will be fatal, a reasonable person might well consider the risk significant and take the appropriate steps to decrease or eliminate it. (I.U.D. v. A.P.I., 448 U.S. 607, 655).

So a risk of 1/1000 (10^{-3}) is clearly significant. It represents the uppermost end of a million-fold range suggested by the Court, somewhere below which the boundary of acceptable versus unacceptable risk must fall.

The Court further stated that ''while the Agency must support its findings that a certain level of risk exists with substantial evidence, we recognize that its determination that a particular level of risk is significant will be based largely on policy considerations.'' The Court added that the significant risk determination required by the OSH Act is ''not a mathematical straitjacket,'' and that ''OSHA is not required to support its findings with anything approaching scientific certainty.'' The Court ruled that ''a reviewing court [is] to give OSHA some leeway where its findings must be made on the frontiers of scientific knowledge [and that] . . . the Agency is free to use conservative assumptions in interpreting the data with respect to carcinogens, risking error on the side of overprotection rather than underprotection'' (448 U.S. at 655, 656).

Nonetheless, OSHA has taken various steps that make it fairly confident its risk assessment methodology is not ''conservative'' (in the sense of erring on the side of overprotection). For example, there are several options for extrapolating human risks from animal data via interspecies scaling factors. The plausible factors range from body weight extrapolation (risks equivalent at equivalent body weights) to (body

weight)$^{2/3}$ (risks equivalent at equivalent surface areas). Intermediate values have also been used, and the value of (body weight)$^{3/4}$, which is supported by physiological theory and empirical evidence, is generally considered to be the midpoint of the plausible values. (Body weight)$^{2/3}$ is the most conservative value in this series. Body weight extrapolation is the least conservative. OSHA has generally used body weight extrapolation in assessing risks from animal data, our approach which tends to be significantly less conservative than the other methodologies and most likely is less conservative even than the central tendency of the plausible values.

Other examples in OSHA's risk assessment methodology where the Agency does not use a conservative approach are selection of the maximum likelihood estimator to parameterize the dose-response function rather than the upper 95% confidence limit, and the use of site-specific tumor incidence rather than pooled tumor response in determining the dose-response function for a chemical agent.

OSHA's overall analytic approach to regulating occupational exposure to particular substances is a four-step process consistent with recent court interpretations of the OSH Act, such as the Benzene decision, and rational, objective policy formulation. In the first step, OSHA quantifies the pertinent health risks, to the extent possible, performing quantitative risk assessments. The Agency considers a number of factors to determine whether the substance to be regulated poses a significant risk to workers. These factors include the type of risk posed, the quality of the underlying data, the plausibility and precision of the risk assessment, the statistical significance of the findings and the magnitude of risk [48 FR 1864, January 14, 1983]. In the second step, OSHA considers which, if any, of the regulatory options being considered will substantially reduce the identified risks. In the third step, OSHA looks at the best available data to set permissible exposure limits that, to the extent possible, both protect employees from significant risks and are also technologically and economically feasible. In the fourth and final step, OSHA considers the most cost-effective way to fulfill its statutory mandate by crafting regulations that allow employers to reach the feasible PEL as efficiently as possible.

B. Review of Data Quality and Statistical Significance

The former OSHA standard for MC was designed to prevent irritation and injury to the neurological system of the employees exposed to MC. In 1985, the National Toxicology Program (NTP) released the results of their MC rodent lifetime bioassays. Those results indicated that MC is carcinogenic to rats and mice. As discussed in the Events Leading to the Final Standard section, based on the NTP findings, EPA now considers MC a probable human carcinogen, and NIOSH regards MC as a potential occupational carcinogen and recommends controlling the exposure to MC to the lowest feasible level. In 1988, ACGIH classified MC as an industrial substance suspected of carcinogenic potential for humans.

As discussed in the Health Effects section, OSHA has determined, based on the NTP data, that MC is a potential occupational carcinogen. This conclusion is supported by high-quality data in both rodent species. Having determined, as discussed in the Quantitative Risk Assessment section, that the NTP study provided suitable data for quantitative analysis, OSHA performed quantitative risk assessments to determine if MC exposure at the current PEL presents a significant risk.

As discussed in the Health Effects and Quantitative Risk Assessment sections, OSHA evaluated four MC rodent bioassays [Exs. 4–35, 4–25, 7–29, 7–30, 7–31] to select the most appropriate bioassay as the basis for a quantitative risk assessment. These bioassays were conducted in three rodent species (rat, mouse, and hamster) using two routes of administration (oral and inhalation). The NTP study (rat and mouse, inhalation) was chosen for a quantitative risk assessment because it provides the clearest toxicological and statistical evidence of the carcinogenicity of MC [Exs. 12, 7–127] and because the studies were of the highest data quality. In the NTP study, MC induced significant increases both in the incidence and multiplicity of alveolar/bronchiolar and hepatocellular neoplasms in male and female mice. In rats, dose-related, statistically significant increases in mammary tumors were also observed. OSHA chose the female mouse tumor response as the basis of its quantitative risk assessment, because of the high quality of data, the clear dose response of liver and lung tumors and the low background tumor incidence. OSHA chose female mouse lung tumors as the specific tumor site for its final quantitative risk assessment. There is no *a priori* reason to prefer the mouse lung tumor response over the liver tumor response because both data sets were of high quality, showed a clear dose-response relationship and had low background tumor incidence. In fact, in the NPRM, the Agency reported estimates of risk generated using both sites. However, to reduce the complexity of the final PBPK analysis, which required highly intensive computations, OSHA chose one site (the female mouse lung tumor response) for its final risk estimates. The risks calculated using the female mouse liver response would likely be only slightly lower than those calculated using the lung tumor response. On the other hand, pooling the total number of tumor-bearing animals having either a lung or liver tumor (or both) would have yielded risk estimates higher than OSHA's final values.

Once the alveolar/bronchiolar neoplasms in female mice were chosen as the most appropriate data set, the multistage model of carcinogenesis was used to predict a lifetime excess risk of cancer from occupational exposure to MC at several concentration levels. The multistage model is a mechanistic model based on the biological assumption that cancer is induced by carcinogens through a series of stages. The model may be conservative, in the sense that it risks error on the side of overprotection rather than underprotection, because it assumes no threshold for carcinogenesis and because it is approximately linear at low doses, although there are other plausible models of carcinogenesis which are more conservative. The Agency believes that this model conforms most closely to what we know of the etiology of cancer. There is no evidence that the multistage model is biologically incorrect, especially for genotoxic carcinogens, which MC most likely is. OSHA's preference is consistent with the position of the Office of Science and Technology Policy which recommends that ''when data and information are limited, and when much uncertainty exists regarding the mechanisms of carcinogenic action, models or procedures that incorporate low-dose linearity are preferred when compatible with limited information'' [Ex. 7–227].

In the NPRM, OSHA solicited comment and testimony on the application of physiologically-based pharmacokinetic (PBPK) modeling to refine the MC risk assessment. There was an intensive discussion of pharmacokinetic issues during the hearings and in comments and briefs submitted to OSHA. PBPK modeling is used to account for metabolic and pharmacokinetic differences between rodents and humans and when extrapolating from high experimental doses to lower occupational exposures. OSHA has evaluated several risk assessments produced using

pharmacokinetic models. Discussion of the major issues surrounding the use of PBPK in risk assessment can be found in the Quantitative Risk Assessment section. Although serious questions remain concerning the application of these models in the MC risk assessment, the Agency has used the estimates generated via PBPK modeling as its final estimate of the carcinogenic risk of MC exposure.

In accepting PBPK analysis, the Agency wanted to be able to utilize all of the data available and appropriate for the analysis. OSHA was also concerned that the uncertainties and inter-individual variabilities in PBPK models were insufficiently quantified to allow analysis of the impact of those uncertainties on the risk. Several rulemaking participants have conducted sensitivity and uncertainty analyses, the most extensive of which was that submitted by Mr. Harvey Clewell on behalf of the U.S. Navy. These analyses show the impact of the variability and uncertainty of the parameters which are used in the PBPK model and suggest methods of quantifying the impact of that uncertainty on the risk estimates.

OSHA has determined that the PBPK data are of sufficient weight to warrant reliance on PBPK modeling to develop a risk estimate in the specific case of MC, a chemical with more extensive information on metabolism than exists for most other substances. To that end, OSHA adopted a Bayesian approach in which all of the physiological and MC-specific data could be used to generate a distribution of estimates of the carcinogenic risks of MC. OSHA used the mean and the upper 95th percentile estimator of the distribution of human PBPK parameters, coupled with the maximum likelihood estimator of cancer potency, to generate its final estimates of risks.

As discussed in more detail in the Health Effects Section above, human data concerning the carcinogenicity of MC were presented in several epidemiology studies. In a study of cellulose triacetate fiber production (MC used as solvent) workers, an increased incidence of liver/biliary cancer [Ex. 7–260] was noted. Although the case numbers were small and the exposure information limited, this epidemiological evidence is consistent with findings from animal studies and indicates that there may be an association between human cancer risk and MC exposure. A study of workers in photographic film production was non-positive [7–163]. However, the exposures experienced by these workers were likely to have been much less than those in the cellulose triacetate fiber plant and, as discussed in the quantitative risk assessment section, the study lacked the power to detect the magnitude of the increase in cancer deaths that would have been predicted given only the bioassay results. A case-control study conducted by the National Cancer Institute showed a statistically significant association between occupational MC exposure and development of astrocytic brain cancer. Exposure levels could not be determined in this study. The results of the epidemiological studies summarized here were not inconsistent with the results of the animal-based cancer potency estimate.

C. Material Impairment of Health

MC is a potential occupational carcinogen. Cancer is a material impairment of health. OSHA has set the 8-hour TWA PEL primarily to reduce the risk to employees of developing cancer.

The STEL of 125 ppm averaged over 15 minutes is primarily designed to protect against MC's non-cancer risks. As discussed in the Health Effects section, there are substantial risks of CNS effects and cardiac toxicity resulting from acute exposure to MC and its metabolites. CNS effects have been demonstrated in workers at concentrations as low as 175 ppm [Ex. 7–153] and a STEL of 125 ppm for 15 minutes would thus be protective against the CNS effects described. Metabolism of MC to CO increases the body burden of COHb in exposed workers. Levels of COHb above 3% COHb may exacerbate angina symptoms and reduce exercise tolerance in workers with silent or symptomatic heart disease. Smokers are at higher risk for these effects because of the already increased COHb associated with smoking (COHb ranges from 2 to 10% in most smokers). Limiting short term exposure to 125 ppm for 15 minutes will keep COHb levels due to MC exposure below the 3% level, protecting the sub-population of workers with silent or symptomatic heart disease and also limiting the additional COHb burden in smokers.

In addition to protecting against CNS and cardiac effects, there is evidence that reducing the GST metabolite production by reducing short term exposure to high concentrations of MC may also lower the cancer risk. This is because metabolism by the MFO pathway (not generally believed to be associated with carcinogenesis) appears to saturate beginning around 100 ppm. This means that exposure to higher concentrations of MC would lead to increased metabolism by the GST pathway (the putative carcinogenic pathway) and therefore, greater than proportionally increased risk.

All of the health effects averted by reducing MC exposure are potentially or likely to be fatal, and this clearly represents ''material impairment of health'' as defined by the OSH Act and case law.

D. Risk Estimates

OSHA's final estimate of excess cancer risks at the current PEL of 500 ppm (8-hour TWA) is 126 per 1000. The risk at the new PEL of 25 ppm is 3.62 per 1000. The risk at 25 ppm is similar to the risk estimated in OSHA's preliminary quantitative risk assessment based on applied dose of MC on a mg/kg/day basis (2.3 per 1000 workers) and clearly supports a PEL of 25 ppm. Risks greater than or equal to 10^{-3} are clearly significant and the Agency deems them unacceptably high. However, OSHA did not collect the data necessary to document the feasibility of a PEL below 25 ppm across all affected industry sectors, and so the Agency has set the PEL at 25 ppm in the final rule. OSHA intends in the future to gather more information pertaining to the feasibility of lower PELs.

E. ''Significant Risk'' Policy Issues

Further guidance for the Agency in evaluating significant risk and narrowing the million-fold range provided in the ''Benzene decision'' is provided by an examination of occupational risk rates, legislative intent, and the academic literature on ''acceptable risk'' issues. For example, in the high risk occupations of mining and quarrying, the average risk of death from an occupational injury or an acute occupationally-related illness over a lifetime of employment (45 years) is 15.1 per 1,000 workers. The typical occupational risk of deaths for all manufacturing industries is 1.98 per 1,000. Typical lifetime occupational risk of death in an occupation of relatively low risk, like retail trade, is 0.82 per 1,000. (These rates are averages derived from 1984–1986 Bureau of Labor Statistics data for employers with 11 or more employees, adjusted to 45 years of employment, for 50 weeks per year).

Congress passed the Occupational Safety and Health Act of 1970 because of a determination that occupational safety and health risks were too high. Congress therefore gave OSHA authority to reduce significant risks when it is feasible to do so. Within this context, OSHA's final estimate of risk from occupational exposure to MC at the current 8-hour TWA PEL (126 per 1000) is substantially higher than other risks

that OSHA has concluded are significant, is substantially higher than the risk of fatality in some high-risk occupations, and is substantially higher than the example presented by the Supreme Court. Moreover, a risk of 3.62 per 1000 at 25 ppm is also clearly significant; therefore, the PEL must be set at least as low as the level of 25 ppm documented as feasible across all industries.

Further, applying the rationale of the Benzene decision, the other risk assessments presented by OSHA and the risk estimates presented by rulemaking participants, including the HSIA (see Table VII–1, below), all support OSHA's conclusion that the human cancer risk for employees exposed to MC above 25 ppm as an 8-hour TWA is significant.

TABLE VII–1.—LIFETIME EXCESS RISK ESTIMATES (PER 1000) FROM OCCUPATIONAL EXPOSURE BASED ON FEMALE MOUSE LUNG TUMOR DATA

Model	MLE (UCL)**		
	25 ppm	50 ppm	500 ppm
OSHA NPRM Risk Assessment (mg/kg/d, BW extrapolation) without PBPK Adjustment	2.32 (2.97)	4.64 (5.92)	45.5 (57.7)
PPM to PPM extrapolation without PBPK Adjustment	11.3 (14.4)	22.4 (28.5)	203 (251)
PBPK Reitz female mouse lung—Reitz human (HSIA assumptions)	0.43 (0.53)	0.93 (1.17)	14.3 (17.9)
PBPK Reitz female mouse lung—Dankovic average human (NIOSH assumptions)	0.81 (1.02)	1.69 (2.12)	15.0 (18.7)
PBPK Clewell female mouse lung—Clewell human (Navy assumptions)*	0.91 (1.14)	1.88 (2.36)	27.5 (34.2)
OSHA Final Risk Assessment (female mouse lung with PBPK)	3.62	7.47	125.8

*Upper 95th percentile of the GST metabolites distribution was used as input in the multistage model.
**Maximum likelihood estimates are 95th percentile upper confidence limit (in parentheses) of the multistage dose-response function.

In addition to being 100 to 1000 times higher than the risk levels generally regarded by other Federal Agencies as on the boundary between significant and insignificant risk (see, e.g., Travis et al., 1987), and 1000 times higher than the ''acceptable risk'' level Congress set in the 1990 Clean Air Act Amendments, the level of 10^{-3} is within the range where economic studies document a marked nonlinearity. In other words, individuals regard risks this high as qualitatively different from ''smaller'' risks. Although risks below 10^{-3} are not unambiguously significant, depending on the size of the affected population, the benefits associated with the risky activity, and other factors, this policy determination is not relevant to this regulation, since OSHA's final risk estimate is substantially greater than 1 per 1000. Risks at or above 10^{-3} are always significant by any empirical, legal or economic argument available.[2]

Because of the lack of documented feasibility data for potential PELs of less than 25 ppm, OSHA has concluded that there is not enough information available to support lowering the 8-hour TWA PEL or STEL further at this time. However, OSHA has integrated other protective provisions into the final standard to further reduce the risk of developing cancer among employees exposed to MC. Employees exposed to MC at the 8-hour TWA PEL limit without the supplementary provisions would remain at risk of developing adverse health effects, so that inclusion of other protective provisions, such as medical surveillance and employee training, is both necessary and appropriate. The action level will encourage those employers for whom it is feasible to do so to lower exposures below 12.5 ppm to further reduce significant risk. Consequently, the programs triggered by the action level will further decrease the incidence of disease beyond the predicted reductions attributable merely to a lower PEL. As a result, OSHA concludes that its 8-hour TWA PEL of 25 ppm and associated action level (12.5 ppm) and STEL (125 ppm) will reduce significant risk and that employers who comply with the provisions of the standard will be taking reasonable steps to protect their employees from the hazards of MC.

The Agency notes that even at the final PELs, the risks to workers remain clearly significant. OSHA will be gathering information on the risks of, and feasibility of compliance with, PELs less than 25 ppm, to determine whether future rulemaking is appropriate in order to further reduce the MC risks to employees.

VIII. Summary of the Final Economic Analysis

In its Final Economic and Regulatory Flexibility Analysis document, OSHA addresses the significant issues related to technological and economic feasibility and small business impacts raised in the rulemaking process. The Final Economic Analysis is also OSHA's most comprehensive explanation of the standard's practical impact on the regulated community; in the Final Economic Analysis, OSHA explains in detail the Agency's findings and conclusions concerning pre-standard (baseline) conditions, such as exposure levels, in establishments in the regulated community, and discusses how and why the requirements of the standard are expected to eliminate significant risk to the extent feasible. This document also sets forth OSHA's Final Regulatory Flexibility Analysis and the analyses required by Executive Order 12866. This Federal Register preamble and the Final Economic Analysis are integrally related and together present the fullest statement of OSHA's reasoning concerning this standard. The Final Economic and Regulatory Flexibility Analysis, together with supporting appendix material, has been placed in the rulemaking docket for methylene chloride (Ex. 129).

The purpose of the Final Economic Analysis is to:

- Describe the need for a standard governing occupational exposure to methylene chloride;
- Identify the establishments and industries potentially affected by the standard;
- Evaluate the costs, benefits, economic impacts and small business impacts of the standard on affected firms;
- Assess the technological and economic feasibility of the standard for affected establishments, industries, and small businesses;
- Evaluate the availability of effective non-regulatory approaches to the problem of occupational exposure to methylene chloride; and
- Present changes designed to reduce the impact of the standard on small

[2] OSHA also conducted an alternative PBPK analysis that uses all of the available human data on MC metabolism, despite the very limited quantity of data available and the additional bias introduced by adopting the ''parallelogram'' assumptions for interspecies scaling (see Quantitative Risk Assessment for a discussion of this analysis and the uncertainties and biases therein). The risk estimate using this alternative method, 1.2 per 1000, is also unambiguously significant.

firms while meeting the objectives of the OSH Act.

Need for the Standard

OSHA's final methylene chloride (MC) standard covers occupational exposures to this substance, one of the most widely used of all organic solvents, in general industry, construction, and shipyard employment. In all, about 237,000 employees are estimated to be exposed to MC. These workers are exposed to MC in many different ways, including the manufacturing, formulation, distribution, and use of MC-containing products. The most common uses of MC are in paint stripping, metal cleaning, and furniture stripping.

Workers exposed to MC are at significant risk of developing cancer, heart and liver effects, and central nervous system impairments, as well as eye, skin, and mucous membrane irritation. Animal bioassays have shown MC to be carcinogenic in mice and rats of both sexes, and epidemiologic studies in workers have produced suggestive evidence of its carcinogenicity in humans. Acute overexposure to the vapors of MC can lead to central nervous system depression, respiratory paralysis, and death: OSHA receives fatality reports every year involving workers who have died using MC to perform such tasks as stripping floors and removing paint. To protect all MC-exposed workers from these adverse health effects, the final standard lowers the airborne concentration of MC to which workers may be exposed from the current permissible exposure limit (PEL) of 500 ppm as an 8-hour time-weighted average (8-hour TWA) to 25 ppm, and from the Agency's current short-term limit of 1000 ppm as an acceptable ceiling, or 2000 ppm as an acceptable peak above the acceptable ceiling for 5 minutes in any 2-hour period, to a short-term exposure limit (STEL) of 125 ppm, averaged over 15 minutes. (For a detailed discussion of the risks posed to workers by exposure to MC, see the Quantitative Risk Assessment and Significance of Risk sections of the preamble, above.)

OSHA's final MC standard is similar in format and content to other health standards issued under Section (6)(b)(5) of the Act. In addition to setting PELs, the standard requires employers to monitor the exposures of workers; establish regulated areas when exposures may reasonably be expected to exceed one of these PELs; implement engineering and work practice controls to reduce employee exposures to MC; provide respiratory protection to supplement engineering controls where these are not feasible, are insufficient to meet the PELs, or in emergencies; provide other protective clothing and equipment as necessary for employee protection; make industrial hygiene facilities (such as eyewash and emergency showers) available in certain circumstances; provide medical surveillance; train workers about the hazards of MC (as required by OSHA's Hazard Communication Standard); and keep records relating to the standard. The contents of the standard are explained briefly in Chapter I of the Final Economic Analysis and in detail in the Summary and Explanation (Section X of the preamble, below).

Chapter II of the economic analysis describes the uses of methylene chloride and the industries in which such use occurs. Employee exposures to MC are analyzed on the basis of ''application groups,'' i.e., groups of firms that use MC to perform a particular function, such as metal cleaning or industrial paint stripping, regardless of the particular industry in which the use takes place. The methodology used by OSHA in the analysis is appropriate when a ubiquitous chemical like MC is used to perform the same function in many kinds of firms in many industries, because the processes used, employee exposures generated, and controls in place or needed to achieve compliance are the same, whether the process takes place in a machine shop, on board ship, or on a construction site. For example, because the process of using MC to strip paint or coatings from an object is essentially the same whether the object being stripped is a spray paint booth, boat, church pew, or automobile, and the exposures generated during the process are similar in important respects, it is appropriate to analyze such activities as a group. However, OSHA's technological feasibility and cost analyses reflect the fact that job classifications and work processes may differ within a given application group. Table VIII–1 shows the application groups analyzed in the economic analysis, and the numbers of MC-using establishments, MC-exposed workers, and estimated volume of MC handled annually by establishments in each application group.

TABLE VIII–1.—METHYLENE CHLORIDE APPLICATION GROUPS

Application group	Estimated number of MC-using establishments *	Estimated total employment *	Estimated number of exposed workers *	Estimated MC handled (millions of lbs)
Methylene Chloride Manufacturing	4	1,664	84	469.20
Distribution/Formulation of Solvents	320	84,004	1,701	189.65
Metal Cleaning:				
Cold Degreasing and Other Cold Cleaning:	23,717	901,232	94,537	32.56
Open-Top Vapor Degreasing	278	27,105	608	14.87
Conveyorized Vapor Degreasing	45	2,920	75	1.13
Semiconductors	239	217,960	1,392	0.40
Printed Circuit Boards	141	77,795	298	13.98
Aerosol Packaging	52	4,142	520	25.21
Paint Remover Manufacturing	80	6,134	200	136.85
Paint Manufacturing	49	8,909	229	3.54
Paint Stripping:				
Aircraft Stripping	300	266,826	2,470	13.17
Furniture Stripping	6,152	23,592	7,872	23.26
Other Industrial Paint Stripping	35,041	2,312,721	46,605	59.36
Flexible Polyurethane Foam Manufacturing	100	9,800	600	50.32
Plastics and Adhesives Manufacturing and Use	3,487	1,186,040	10,481	41.90
Adhesive Production	165	56,254	497	.....
Adhesive Use	1,753	596,291	5,269	.....
Injection Molding	80	27,211	240	.....

TABLE VIII–1.—METHYLENE CHLORIDE APPLICATION GROUPS—Continued

Application group	Estimated number of MC-using establishments *	Estimated total employment *	Estimated number of exposed workers *	Estimated MC handled (millions of lbs)
Lamination	1,323	450,031	4,070	.....
Mold Release	165	56,254	497	.....
Ink Use:				
Ink and Ink Solvent Manufacturing	15	2,010	58	3.68
Ink Solvent Use in Printing	11,869	197,619	39,481	3.68
Pesticide Manufacturing and Formulation	60	1,440	120	9.58
Pharmaceutical Manufacturing	108	70,223	1,431	39.53
Solvent Recovery	34	932	137	32.10
Film Base Manufacturing	1	45,000	500	8.90
Polycarbonate Manufacturing	4	1,898	67	6.70
Construction	9,504	63,115	24,896	2.44
Shipyards	25	85,212	3,040	0.47
Total, all application groups	91,624	5,598,293	237,496	**

* In most cases, the estimated number of establishments in each application group was based on the volume flow of MC in 1990 divided by the estimated MC use per facility. The estimated number of establishments was multiplied by the total number of employees per establishment and exposed employees per establishment as reported in CONSAD's survey.

** Netting out rehandling, estimated total consumption equals 469.2 million pounds manufactured, minus 129.1 million pounds exported, + 19.3 million pounds imported, + 32.10 million pounds recovered from used solvent. The column does not sum to 391.5 million pounds because non-consumptive uses such as production, distribution and formulation, and solvent recovery are included.

Sources: CONSAD, HSIA, PRMA, Office of Regulatory Analysis.

In all, OSHA analyzed 28 application groups. These application groups include, among others, methylene chloride manufacturing, paint manufacturing, metal cleaning, polyurethane foam manufacturing, plastics and adhesives manufacturing, ink use, pharmaceuticals, and construction and shipyards. A total of 91,624 establishments are estimated to be potentially affected by the standard. These establishments employ a total of 5.6 million employees, of whom 237,496 are estimated to be exposed to MC in the course of their work. The application groups with the largest numbers of directly exposed employees are the Metal Cleaning, All Other Industrial Paint Stripping, and Ink Solvent Use groups. In many facilities, MC is used only by a small number of employees; the average number of MC-exposed employees per establishment covered by the final rule is only 2.6 employees.

Chapter III of the analysis assesses the technological feasibility of the final standard's requirements, and particularly its PELs, for firms in the 28 application groups identified in the Industry Profile. OSHA finds, based on an analysis of exposure data taken on workers performing the MC-related tasks identified for each application group, that compliance with the standard is technologically feasible for establishments in every application group studied. With few exceptions, employers will be able to achieve compliance with both PELs through the use of engineering controls and work practices. The few exceptions are certain maintenance activities, such as vessel cleaning, which have traditionally involved the use of respiratory protection, and operations in two applications where the supplemental use of respirators may be necessary. These operations are centrifuge unloading and dryer loading at one bulk pharmaceutical manufacturing facility operated by Abbott Laboratories, and operations involving access to and entering of the roll coating machine used by the Eastman Kodak Company to make film base.

The exposure data relied on by OSHA in making its technological feasibility determinations have been compiled in a database that contains thousands of MC exposure results (see Appendix B of this analysis) taken by OSHA compliance officers, consultation program consultants, MC-using companies, and interested parties. These data show that many facilities in many of the affected application groups have already achieved the reductions in employee exposures required by the final rule. In addition, the exposures of many employees in many job categories in a number of the application groups have been reduced to levels that are close to those required by the standard. OSHA's analysis of technological feasibility analyzes employee exposures at the operation or task level to the extent that such data are available. In other words, the analysis identifies relevant exposure data on a job-category-by-job category basis to permit the Agency to pinpoint those MC-exposed workers and job operations that are not yet under good process control and will thus need additional controls (including improved housekeeping, maintenance procedures, and employee work practices) to achieve compliance. Costs are then developed (see Chapter V of the economic analysis) for the improved controls needed to reach the new levels.

The benefits that will accrue to MC-exposed employees and their employers are substantial and take a number of forms. Chapter IV of the analysis describes these benefits, both in quantitative and qualitative form. First, based on a physiologically-based pharmacokinetic (PBPK) model, OSHA estimated that, if all 237,000 employees were exposed at the existing 8-hour TWA exposure limit of 500 ppm for an occupational lifetime of 45 years, a total of 29,862 excess cancer deaths would occur, or 126 excess cancer deaths per 1,000 workers. If, however, the 237,000 employees were exposed to the final standard's PEL of 25 ppm for 45 years, 8533 excess cancer deaths would be expected (3.6 per thousand workers). However, few workers are currently being exposed to 500 ppm of MC as an 8-hour TWA. The actual exposure levels of most affected workers are considerably lower, and, when these exposure levels, rather than 500 ppm, are used as the baseline, the PBPK model estimates that 1405 cancer deaths will be averted over a 45-year period. By reducing the total number of MC-related cancer deaths from 1,804 deaths to 399 deaths over 45 years, the standard will

save an average of 31 cancer deaths per year. Table VIII–2 shows these risk estimates.

TABLE VIII–2.—LUNG CANCER RISK OVER 45 YEARS FOR WORKERS EXPOSED AT CURRENT EXPOSURE LEVELS AND AT THE LEVELS EXPECTED AFTER IMPLEMENTATION OF THE FINAL STANDARD

	0–12.5	12.5–25	25	25–50	50–100	100–200	200–350	350–500	500+***	Total
Lifetime Excess Cancer Risk (per thousand workers)*	0.91	2.71	3.60	5.53	11.98	28.45	61.75	104.44	125.78	.....
Baseline Number of Workers Exposed	141,323	26,464	162	22,839	23,903	14,803	3,281	1,297	3,422	237,495
Estimated Excess Deaths in Baseline (Existing PEL)**	129	72	1	126	286	421	203	135	430	1,804
Predicted Number of Workers Exposed at New PEL	159,825	28,441	49,229	0	0	0	0	0	0	237,495
Predicted Excess Deaths at New PEL**	146	77	176	0	0	0	0	0	0	399

*Based on OSHA's final estimate using the PBPK model, as presented in the Quantitative Risk Assessment section of the Preamble.
**Computed as level of lifetime risk times the number of exposed workers.
***For workers exposed to levels of greater than the current PEL of 500 ppm, the risk estimate is that associated with a lifetime exposure to 500 ppm.
Source: Office of Regulatory Analysis; OSHA; Department of Labor.

In addition to cancer deaths, the standard is estimated to prevent 3 deaths per year from MC's acute central nervous system and carboxyhemoglobinemic effects. (Carboxy-hemoglobinemia is the inability of the blood to carry sufficient oxygen to supply the heart muscle; because methylene chloride interferes with the blood's ability to carry oxygen, exposure to it places susceptible individuals, such as those with silent cardiovascular disease, pregnant women, and smokers, at greater risk.) OSHA receives reports every year of workers who have succumbed to MC's acute CNS toxicity while they were engaged in such tasks as floor stripping. For example, the Agency recently received a fatality report on two young workers who died after pouring 14 gallons of MC on a squash court they were refinishing. Both of these employees lost consciousness, collapsed, and subsequently died of respiratory failure. In addition, MC exposures above the level at which the final rule's STEL is set—125 ppm—are also associated with acute central nervous system effects, such as dizziness, staggered gait, and diminished alertness, all effects that can lead to workplace accidents. OSHA estimates that as many as 30,000 to 54,000 workers will be protected by the final rule's STEL from experiencing CNS effects and episodes of carboxyhemoglobinemia every year. Moreover, exposure to the liquid or vapor forms of MC can lead to eye, skin, and mucous membrane irritation, and these material impairments will also be averted by compliance with the final rule. Finally, contact of the skin with MC can lead to percutaneous absorption and systemic toxicity and thus lead to additional cases of cancer that have not been taken into account in the benefits assessment presented in Chapter IV of the Final Economic Analysis.

The costs employers in the affected application groups are estimated to incur to comply with the standard total $101 million in 1994 dollars. These costs, which are presented in Chapter V of the full economic analysis, are annualized over a 10-year horizon at a discount rate of 7 percent. Table VIII–3 shows annualized costs by provision of the standard; the most costly

provisions are those requiring engineering controls, protective clothing and eye protection, and medical surveillance for MC-exposed workers. These three provisions together account for approximately 75 percent of the standard's compliance costs.

TABLE VIII–3.—ANNUALIZED COSTS BY PROVISION

Provision	Annualized Costs
Engineering Controls	$38,773,642
Respirators	6,374,083
Monitoring	9,849,577
Protective Clothing and Eye Protection	29,578,340
Emergency Eyewash and Shower	3,183,486
Medical Surveillance	7,986,493
Leak and Spill Detection Program	3,703,286
Regulated Areas	150,884
Recordkeeping	652,121
Training	196,656
Understanding Regulation and Developing Training	777,132
Subtotal	101,225,701
Costs of Substitution	237,336
Total	101,463,037

Source: Office of Regulatory Analysis; OSHA; Department of Labor.

Table VIII–4 analyzes compliance costs by application group and shows that the Cold Cleaning application group, which is in the larger Metal Cleaning grouping, and the Furniture Stripping application group, which is in the larger Paint Stripping category, will incur the largest costs of compliance (though not necessarily the largest economic impacts). These costs reflect the high exposures and relative lack of control measures currently existing in many establishments in these two application groups. In other words, because MC exposures are poorly controlled in so many cold cleaning and furniture stripping facilities, employers in these industries will be required by the standard to implement control measures to protect their employees from the significant risk of MC exposure.

TABLE VIII–4.—ANNUALIZED COSTS BY METHYLENE CHLORIDE APPLICATION GROUPS

Application group	Annualized costs
Methylene Chloride Manufacturing	8,150
Distribution/Formulation of Solvents	794,099
Metal Cleaning:	
Cold Degreasing and Other Cold Cleaning	26,950,869
Open-Top Vapor Degreasing	371,096
Conveyorized Vapor Degreasing	97,253
Semiconductors	247,666
Printed Circuit Boards	217,479
Aerosol Packaging	297,999
Paint Remover Manufacturing	229,724
Paint Manufacturing	89,697
Paint Stripping:	
Aircraft Stripping	8,148,754
Furniture Stripping	10,689,840
All Other Industrial Paint Stripping	24,413,924
Flexible Polyurethane Foam Manufacturing	4,252,861
Plastics and Adhesives Manufacturing and use	5,417,950
Adhesive Production	
Adhesive Use	
Injection Molding	
Lamination	
Mold Release	
Ink and Ink Solvent Manufacturing	23,518

TABLE VIII–4.—ANNUALIZED COSTS BY METHYLENE CHLORIDE APPLICATION GROUPS—Continued

Application group	Annualized costs
Ink Solvent Use	3,360,723
Pesticide Manufacturing and Formulation	106,060
Pharmaceutical Manufacturing	311,708
Solvent Recovery	49,829
Film Base Manufacturing	47,454
Polycarbonate Manufacturing	4,651
Construction	14,922,000
Shipyards	518,544
Total, all application groups	101,463,037

Source: Office of Regulatory Analysis; OSHA; Department of Labor.

Chapter VI of the economic analysis analyzes the impacts of compliance costs on firms in affected application groups. The standard is clearly economically feasible: on average, annualized compliance costs amount only to 0.18 percent of estimated sales and 3.79 percent of profits. For all but three application groups—polyurethane foam blowing, furniture stripping, and construction—compliance costs are less than 3 percent of profits, and for all but one application group—furniture stripping—annualized compliance costs are less than 0.5 percent of the value of sales. Table VIII–5 shows average compliance cost impacts across the many Standard Industrial Classification (SIC) codes potentially involved in the application groups studied.

TABLE VIII–5.—SCREENING ANALYSIS TO IDENTIFY POSSIBLE ECONOMIC IMPACT OF THE FINAL MC STANDARD

Application group	Number of establishments complying	Annualized costs of compliance	
		As percent of sales	As percent of profit
Manufacture of MC	4	(*)	0.04
Distribution/Formulation of Solvents	320	0.04	0.55
Metal Cleaning:			
Cold Degreasing and Other Cold Cleaning	23,717	0.01	0.18
Open-Top Vapor Degreasing	278	0.01	0.22
Conveyorized Vapor Degreasing	45	0.02	0.35
Semiconductors	239	(*)	0.05
Printed Circuit Boards	141	0.02	0.41
Aerosol Packaging	50	0.01	0.13
Paint Remover Manufacturing	80	0.02	0.06
Paint Manufacturing	49	0.01	0.04
Paint Remover Use (Paint Stripping):			
Aircraft Stripping (Large Firms)	75	0.07	1.34
Aircraft Stripping (Small Firms)	225	0.08	2.12
Furniture Stripping	6,152	2.04	**39.40

TABLE VIII–5.—SCREENING ANALYSIS TO IDENTIFY POSSIBLE ECONOMIC IMPACT OF THE FINAL MC STANDARD—Continued

Application group	Number of establishments complying	Annualized costs of compliance	
		As percent of sales	As percent of profit
All Other Industrial Paint Stripping	35,041	0.01	0.11
Flexible Polyurethane Foam Manufacturing	100	0.32	**9.23
Plastics and Adhesives Manufacturing and Use	3,487	0.03	0.52
Ink and Ink Solvent Manufacturing	15	(*)	0.03
Ink Solvent Use	11,869	0.03	0.05
Pesticide Manufacturing and Formulation	60	0.01	0.35
Pharmaceutical Manufacturing	108	(*)	0.03
Solvent Recovery	37	0.05	0.85
Film Base	1	(*)	0.01
Polycarbonates	4	(*)	(*)
Construction	9,504	0.35	**9.67
Shipyards	25	0.07	1.72
All Application groups	91,625	0.18	3.79

* = less than .005%.

** These relatively high impacts on profits assume that no price increase is possible. In all three cases, price increases of 2.1 percent or less would fully restore profits. In all of these application groups, most firms will be able to increase prices to offset their regulatory costs. In furniture stripping, a substantial portion of the market is for antique refinishing that involves MC use, a service which is relatively price insenstive. Soft flexible foam of the kind MC is used to make is an essential material in the construction of cushions of all types. In the construction sector, MC based paint stripping and foam blowing are essential operations of many of the jobs in which they are used.

SOURCES: CONSAD; Dun & Bradstreet; Office of Regulatory Analysis, OSHA, Department of Labor.

It is important to understand that OSHA's methodology tends to overestimate the economic impacts of the standard, for a number of reasons. For example, OSHA's cost methodology does not take into account the many simple and virtually cost-less improvements in employee work practices and housekeeping procedures that would enable many employers to achieve compliance with the final rule's PELs. In flexible polyurethane foam manufacturing, for example, OSHA's costs may be overestimated because it was assumed that no firms would substitute away from MC entirely, even though some firms have already done so (as described in Chapter III, Technological Feasibility). Despite the fact that OSHA's cost estimates are likely to be overestimates, OSHA decided to examine in greater detail the three application groups shown by the economic analysis to have the highest costs as a percentage of profits, i.e., furniture stripping, polyurethane foam manufacturing, and construction.

In the furniture refinishing application group, compliance costs are 2.0 percent of the value of revenues and 39 percent of the value of before-tax profits. Approximately half of all furniture refinishing sales derive from antique refinishing, a market niche that is unlikely to be sensitive to a 2.0 percent change in price. Even in the area of used furniture refinishing, which constitutes the remaining half of the furniture refinishing market, a 2.0 percent price increase would be unlikely to significantly alter the amount of furniture being refinished. In general, price increases of this magnitude would be expected to result only in a very small drop in the demand for furniture refinishing. If this were not the case, normal business fluctuations, such as drops in the relative cost of new furniture or a major increase in the price of methylene chloride (such as has occurred in recent years) would also have had major impacts on the industry.

In construction and polyurethane foam manufacturing, compliance costs for the average firm are 9.2 and 9.7 percent of profits, respectively. However, to offset these costs, construction firms would need only to increase their revenues by 0.35 percent and foam blowing operations would need only to increase the price of their products by 0.32 percent. In construction, such price increases are unlikely to present a problem, since the use of MC is essential on many larger construction projects. For example, it is difficult to believe that demand for remodeling or renovation projects would be seriously altered by a 0.35 percent increase in the cost of the paint stripping portion of the job. In flexible polyurethane foam manufacturing, either MC or an appropriate substitute is essential to the production of low density, or soft, foam, and foam, in turn, is essential to the production of many kinds of furniture. Demand for such products is unlikely to change as a result of an 0.32 percent increase in the price of flexible foam. OSHA therefore concludes that even marginal firms in these three sectors—furniture stripping, construction, and flexible foam blowing— are unlikely to close as a result of the compliance costs of this standard.

To ensure that the analysis of average impacts presented in the economic analysis did not obscure potentially significant economic impacts at the 4-digit SIC level, OSHA performed an in-depth analysis of the 4-digit SICs potentially involved in the Cold Cleaning and All Other Industrial Paint Stripping application groups. The results of this in-depth analysis are presented in Appendix D of the full economic analysis. In all, a total of 162 4-digit SICs potentially impacted by the standard in the Cold Cleaning group and more than 200 4-digit SICs in the Other Industrial Paint Stripping group were analyzed. Across all of the Cold Cleaning SICs, the average impact of the costs of compliance is 0.06 percent of revenues and 1.12 percent of profits. The largest impacts on profits occur in SIC 3412, Metal Barrels, Drums, and Pails, and SIC 3494, Valves and Pipe Fittings not elsewhere classified; in these cases, impacts on profits are 13.3 and 15.1 percent, respectively. In both of these cases, however, these impacts are explained by extremely low profit margins (less than .02 percent of sales, i.e., less than $2 per $10,000 in sales, in 1994). As a result, a price increase of less than one cent per $100 of revenue would leave profits unchanged. Such a price increase is feasible because an

increase of this magnitude is unlikely to lead to significant changes in the demand for metal barrels or valves and pipe fittings. In no other 4-digit Cold Cleaning SIC did impacts reach even 5 percent of profits.

Across all 200-plus Industrial Paint Stripping SICs, the average impact of the costs of compliance on revenues is 0.03 percent. The largest impact of costs on sales is 0.33 percent and occurs in SIC 7532, Auto Top, Body Repair, and Paint Shops (discussed further below). The average impacts of costs on profits across these SICs is 0.17 percent. The largest impacts on profits occur in SIC 3412, SIC 3494 (both discussed above), and in SIC 7532, Auto Tops, Body Repair and Paint Shops; in all three of these SICs, cost impacts are between 6 and 8 percent of profits. Again, the explanation for these impacts in SICs 3412 and 3494 is that their profit margin in 1994 was vanishingly low. The resulting price increases required to maintain profits are also extremely small, and OSHA concludes that such an increase is likely to take place in these cases. In SIC 7532, the other relatively high impact SIC, profit margins are relatively high (approximately 4.4 percent), and thus a small decline of this magnitude would have relatively little impact.

Summary of the Regulatory Flexibility Analysis

In its 1991 proposal, OSHA requested comments and information that would assist the Agency in identifying small-business users of MC and in structuring the final standard so that these users would be able to achieve the standard's worker protection goals in ways that would be technologically and economically feasible for them (56 FR 57041 to 57043). OSHA anticipated that, as stated in the proposal, the standard might have a significant economic impact on small entities in at least two application groups: firms with fewer than 20 employees that engage in stripping of paint from aircraft, and firms with fewer than 20 employees that engage in furniture stripping.[3] OSHA also requested comment concerning the standard's impact on small employers in light of the Regulatory Flexibility Act's mandate to consider and minimize impacts on small businesses, consistent with the purposes and criteria of the standard's enabling legislation (56 FR 57115 to 57121).

Many commenters identified additional application groups that include small establishments likely to have difficulty achieving all of the standard's protective goals if the requirements of the standard were structured in a one-size-fits-all manner. These commenters provided considerable data and identified many possible modifications and alternatives to the proposed standard that they believed would facilitate compliance and mitigate the standard's impact on MC-using establishments with fewer than 20 employees.

None of the comments concerning small employer issues, whether in the context of economic or technological feasibility or the Regulatory Flexibility Act, disagreed with OSHA's basic premise that the fewer-than-20-employee cut-off was appropriate to distinguish between large and small MC-using businesses, was a useful way of characterizing the compliance abilities and limitations of affected employers and is an appropriate definition for purposes of the Regulatory Flexibility Act. Use of this numerical cut-off point captures 61 percent of all establishments potentially affected by the final rule. MC-users with fewer than 20 workers tend to have the characteristics of ''mom-and-pop'' businesses, whereas establishments with 20 or more workers are generally more sophisticated in terms of the technology they use and their management resources. The 20-employee threshold has also proved to be an agreed-on and useful cut-off point in past OSHA rulemakings (see, for example, the permit-required confined spaces standard (58 FR 4547) and the process safety management standard (57 FR 6402)).

During Executive Order 12866 review, the Office of Advocacy of the Small Business Administration expressed its views concerning OSHA's small business definition. In a letter to OMB, the SBA's Chief Counsel for Advocacy stated in a letter dated August 16, 1996, that ''[t]he regulatory alternatives developed, using OSHA's size standard of less than 20 employees, were somewhat beneficial to two of the three industries [furniture stripping, polyurethane foam blowing, and construction]. These industries, i.e., furniture stripping and construction, are predominantly micro businesses that fall into OSHA's definition of small'' (Ex. 130). The Office of Advocacy was concerned, however, that the 20-employee cut-off did not adequately deal with the MC-using polyurethane foam manufacturing sector. (In this application group, the majority of establishments likely to experience significant economic impacts fall into the 20 to 99- employee size category.) ''[T]he characteristics of the manufacturing sector indicate that the [20 employee] size standard was not appropriate in that industry for the purposes of regulatory flexibility.'' *Id*. The SBA concluded that OSHA should consider taking additional steps to address implementation burdens and the needs of the polyurethane foam manufacturing sector.

Working with OMB and the SBA's Office of Advocacy to resolve this concern, OSHA reexamined the potential impacts of the standard on polyurethane foam manufacturing establishments in the 20 to 99 employee size category in the context of economic impact issues. As explained more fully in the Final Economic and Regulatory Flexibility Analysis, OSHA concluded that, even though members of this group were not small employers, some accommodation would be necessary to assure that employees working in establishments of this size in this industry would not receive less protection than all other MC-exposed employees. Accordingly, OSHA extended the engineering control implementation date for this group of establishments by one year. This extended phase-in is designed to enable this group of employers to plan for and accumulate the capital to finance needed controls, install them, and ensure their effective and consistent operation before the compliance deadline.

OSHA's extensive feasibility studies and focus on small business issues resulted in a number of modifications that have made the standard more cost-effective for business while maintaining protection for workers. In addition, OSHA conducted an alternative screening analysis to measure the final rule's potential impacts on establishments in the regulated community using the SBA's size standards. For most application groups, this meant that OSHA examined the standard's economic impacts on firms at the 500 employee level. (Financial data are not available for cut-off points higher than 500 employees; thus, OSHA used that cut-off for all application groups.) In some cases, the SBA size standards are defined in terms of annual revenues, and for SICs so defined, OSHA translated these revenue figures into the appropriate employee size category. This SBA-based alternative screening analysis enabled the Agency to determine whether, by failing to look

[3] As a result of data and information received from commenters and other information in the record, the Final Economic Analysis does not identify significant impacts or technologic or economic feasibility problems for aircraft stripping operations of any size.

at potential impacts among firms in other size classes, significant impacts had been overlooked. The analysis conducted using the SBA size standards confirmed that any potentially significant economic impacts associated with the final rule occur among firms in the fewer-than-20-employee category, with one exception, i.e., firms in the 20–99 employee size category in the polyurethane foam manufacturing industry. (See the full Final Economic Analysis for additional detail.)

For the final rule, OSHA has analyzed the costs of compliance as a percentage of profits, and costs as a percentage of revenues, for firms with fewer than 20 employees in every application group. This analysis identified significant economic impacts on a substantial number of small entities, and the Agency has accordingly conducted a full Final Regulatory Flexibility Analysis in accordance with the Regulatory Flexibility Act, as amended in 1996. The three application groups for which such impacts were identified were Furniture Stripping, Polyurethane Foam Blowing, and Construction. Table VIII–6 shows the results of this analysis in detail.

The full regulatory flexibility analysis is presented in Chapter VI of the Final Economic and Regulatory Flexibility Analysis. The remainder of this section briefly summarizes that analysis.

This rule is needed to prevent cancer deaths and other illnesses, as discussed in greater detail in the Health Effects Section (Section V of this Preamble). Section III of this preamble, Events Leading to the Final Standard, summarizes OSHA's efforts to assure input to this rulemaking by affected small firms. Table VIII–6 identifies the affected small firms by sector. OSHA estimates that a total of 56,000 small firms will be affected by this standard.

TABLE VIII–6.—SCEENING ANALYSIS OF POTENTIAL ECONOMIC IMPACTS ON SMALL FIRMS

Application group	Number of small establishments affected	Costs as a percentage of profits for small firms	Costs as a percentage of sales for small firms
Manufacture of MC	0	NA	NA
Distribution/Formulation of Solvents	139	3.0%	0.2
Metal Cleaning:			
Cold Degreasing and Other Cold Cleaning	9,223	0.9	0.0
Open-Top Vapor Degreasing	0	NA	NA
Conveyorized Vapor Degreasing	11	2.4	0.1
Semiconductors	0	NA	NA
Printed Circuit Boards	20	2.0	0.1
Aerosol Packaging	10	0.7	0.1
Paint Remover Manufacturing	34	0.3	0.1
Paint Manufacturing	7	0.1	0.0
Paint Remover Use (Paint Stripping):			
Aircraft Stripping (Large Firms)	0	NA	NA
Aircraft Stripping (Small Firms)	75	4.5	0.1
Furniture Stripping	5,901	41.5*	2.2
All Other Industrial Paint Stripping	25,441	0.8	0.0
Flexible Polyurethane Foam Manufacturing	8	60.3*	1.7
Plastics and Adhesives Manufacturing and Use	498	1.8	0.1
Ink and Ink Solvent Manufacturing	3	NA	NA
Ink Solvent Use	5,395	0.1	0.1
Pesticide Manufacturing and Formulation	40	6.6	0.2
Pharmaceutical Manufacturing	0	NA	NA
Solvent Recovery	17	2.7	0.1
Film Base	0	NA	NA
Polycarbonates	0	NA	NA
Construction	9,085	19.9*	0.5
Shipyards	0	NA	NA
All Application groups	55,908	8.2	0.3

NA=No small firms in this application group.

*These relatively high impacts on profits assume that no price increase is possible. In all three cases, price increases of 2.1 percent or less would fully restore profits. In all of these application groups, most firms will be able to increase prices to offset their regulatory costs. In furniture stripping, a susbtantial portion of the market is for antique refinishing that involves MC use, a service which is relatively price insensitive. Soft flexible foam of the kind MC is used to make is an essential material in the construction of cushions of all types. In the construction sector, MC based paint stripping and foam blowing are essential operations of many of the jobs in which they are used.

Sources: CONSAD; Dun & Bradstreet; Office of Regulatory Analysis, OSHA, Department of Labor.

The Summary and Explanation section of this preamble provides a description of the compliance requirements associated with this rule, and a paperwork burden analysis of the record keeping requirements is provided in the Collection of Information Request for Comment section at the beginning of this preamble. Based on comments regarding anticipated effects on small businesses, OSHA has reduced the final rule's overall paperwork requirements from those proposed and has refined some paperwork requirements to simplify compliance for small entities.

OSHA considered numerous regulatory alternatives and modifications to the requirements of the proposed standard (ranging from higher PELs, to 40-hour rather than 8-hour time weighted average exposure limits, to delayed implementation dates) that commenters believed might minimize significant economic impacts on small businesses. OSHA rejected those alternatives that clearly decreased the safety of workers in small establishments, but the Agency also adopted many regulatory changes that will improve small employers' ability to provide their employees with the same level of protection as that afforded workers in larger establishments. As

explained more fully in the Final Economic Analysis and summarized in Table VIII–7, the final standard contains delayed implementation dates, reduced paperwork requirements, streamlined medical surveillance provisions and other accommodations that, in the Agency's judgment, will minimize any significant economic impacts of the standard on small employers to the extent necessary to enable them to meet the standard's protective goals.

TABLE VIII–7. CHANGES MADE SINCE THE PROPOSED REGULATION TO REDUCE THE FINAL STANDARD'S IMPACTS ON SMALL BUSINESSES

Change to proposed regulation	Impact on small businesses
Firms with fewer than 20 employees given 3 years (rather than 1) to achieve PEL using engineering controls.	More performance oriented and flexible, reduces costs to small businesses in first two years by 30 to 40 %, allows small businesses time to plan major expenditures.
Allows the use of licensed health care professionals in addition to physicians for medical surveillance.	Provides greater flexibility.
Laboratory tests are at the discretion of physician rather than automatically required.	Reduces costs of medical surveillance by more than 14 percent, more performance oriented.
Employees under 45 are required to have a physical every three years rather than annually.	Reduces costs of medical surveillance by 30 percent.
Respirators required in regulated areas only when PEL is likely to be exceeded.	Decreases respirator use and costs for small business.
If MC is used less than 30 days per year, monitoring may be conducted with direct reading instruments.	Significantly reduces costs of monitoring for establishments making limited use of MC; this provision will be especially helpful in construction.
Written compliance plans are no longer required	Reduces paperwork.
Hazard communication requirements do not go beyond what is already required by hazard communication standard.	Reduces paperwork and costs.
Employee re-training only as needed rather than annually	More performance oriented, reduces costs of training 80 percent.
Simplified recordkeeping for small businesses for exposure monitoring data.	Reduces paperwork.

IX. Environmental Impact

This section analyzes the impact on the environment of changing the standard for methylene chloride (MC) to an eight-hour time weighted average (TWA8) permissible exposure limit (PEL) of 25 parts per million (ppm), with a 125 ppm 15-minute short-term exposure limit (STEL) and ancillary requirements. It is based principally on information collected for OSHA by CONSAD Research Corporation and its subcontractor, PEI Associates Inc., and reported in *Economic Analysis of Draft Regulatory Standard for Methylene Chloride,* 1990, OSHA Docket, Ex. 15, and also draws upon other materials in the OSHA docket.

Current uses of methylene chloride involve releases to the air through venting of storage tanks or drums and through evaporation of MC during the performance of various activities such as paint stripping and cold cleaning indoors or outdoors. The volume of MC emitted as a percentage of MC used varies greatly among industries. Some processes, such as polyurethane foam manufacturing and paint stripping, typically release 100 percent of the MC to the atmosphere (Ex. 15). Other uses, such as solvent recovery and the manufacture of methylene chloride, involve less than 1 percent of the MC used being emitted to the atmosphere (Ex. 15). In addition, air, water, or solid waste pollution may occur as a result of the disposal of waste residues containing MC. Additional details by application group are presented in CONSAD's report [Ex. 15].

Future environmental releases of methylene chloride resulting from the final standard will largely be a function of how it affects the demand for methylene chloride and for its substitutes. The demand for methylene chloride has been declining (e.g., generally, it is no longer being used in formulating hairsprays). Any regulatory action by OSHA is expected to further reduce the demand for MC and thus the extent of its environmental releases.

Although it is technically possible to substitute chlorofluorocarbons (CFCs) for methylene chloride in electronics and foam blowing, OSHA does not expect the revision of the MC standard to have any such effect. CFC products are significantly more expensive than MC products and are themselves being phased out or banned because of their effects on the environment.

To the extent that firms might have to use greater quantities of substitute chemicals to get the same effects formerly obtained with MC, waste residues and disposal costs would increase. On the other hand, increases in MC leak prevention and recycling would improve the environment.

The Paint Remover Manufacturers Association (PRMA) has charged that the standard would cause ''massive amounts'' of methylene chloride to be emitted into the atmosphere (Ex. 19–11). In Chapter III, OSHA noted that it could find no convincing argument by PRMA as to why the total amount emitted after installation of exhaust ventilation would differ significantly from the amount now simply leaking into the atmosphere.

At informal public hearings, PRMA stated that ''an exposure level of 25 PPM is so low that it brings into the issue the formation of vapor clouds with levels of greater than 25 PPM that could move in and around the neighborhood,'' allegedly through decomposition of the MC [Tr. 245, 9/17/92]. There is no evidence that this hypothetical situation has ever occurred. PRMA may have confused decomposition with diffusion [Tr. 940–941, 9/21/92]. At Eastman Kodak Company, which currently emits more methylene chloride into the atmosphere than any furniture stripper possibly could, the chemical has diffused so rapidly that no clouds of MC have been formed [Tr. 1237–1238, 9/22/92].

Generally, it is not expected that any significant environmental impact will result from revision of the methylene chloride standard.

X. Summary and Explanation of the Final Standard

Introduction

The final standard for occupational exposure to methylene chloride (MC) is different in several important respects from the proposed MC standard

published in the Federal Register in 1991 (56 FR 57036). For example, the standard has been written in plain language, is more performance-oriented than the proposal, and substantially reduces the amount of paperwork employers will have to complete. Employers will thus find compliance with the standard easier, their paperwork less extensive, and their obligations clearer and less burdensome. These changes are discussed in greater detail in the appropriate sections of this Summary and Explanation. OSHA seeks input from users of the standard on whether these changes are helpful and what other changes could be made to future standards to increase their user-friendliness. OSHA will also be conducting a number of compliance assistance and outreach projects in connection with this standard to assist employers and employees to comply.

As part of the Agency's new approach to standards writing, OSHA has included an introductory paragraph in the standard to provide readers with information on MC, its health effects and principal uses, and the reasons OSHA is regulating this toxic substance. This introductory language is non-mandatory and is intended only to provide information and enhance compliance.

This final rule is an occupational health standard that establishes requirements to control employee exposure to MC, a chemical compound found in many different types of industries. OSHA has determined that this standard is necessary because exposure to MC places employees at significant risk of developing exposure-related adverse health effects. These effects include cancer, effects on the heart and central nervous system, and skin and eye irritation. Employee exposure to MC can occur through inhalation or through skin absorption or contact with the skin. This substance is frequently used as a solvent in many different kinds of jobs, including furniture stripping, foam blowing, film manufacturing and metal degreasing.

Although the final rule covers many different types of workplaces where MC is used, the extent of coverage depends on the magnitude of employee exposure. Although all covered employers, i.e., those with MC in the workplace, must determine initially the extent to which their employees are exposed to MC, those with exposures at or below the action level will only have to document the results of this initial determination, provide employee information and training, and provide means of protecting employees from contact with liquid MC. The standard's other requirements, such as those for engineering controls, medical surveillance, etc. apply only to workplaces where employee exposures to MC exceed the action level.

Paragraph (a) Scope and application

This standard applies to all occupational exposures in workplaces covered by OSHA in general industry, construction and shipyards where MC is produced, released, stored, handled, or used.

As discussed in the Health Effects and Significance of Risk sections of this preamble, OSHA has determined that exposure to MC at the former PEL creates a significant risk that employees' health will be materially impaired. Possible adverse health effects include cancer, cardiac effects, central nervous system effects, and skin or eye irritation. Exposures to MC are found in various general industry, construction, and shipyard facilities, and OSHA has determined that there are feasible measures to control them in each of these types of employment.

In the proposal's Authority section, OSHA preliminarily determined, under Section 4(b)(2) of the OSH Act, that it would be appropriate for the MC standard to supersede any corresponding longshoring standards in § 1910.16 and 29 CFR part 1918. The Agency therefore proposed to add a new paragraph (m) to § 1910.19. In addition, in questions raised by the Agency in its Notice of Public Hearing, OSHA requested input regarding the use of MC in longshoring. However, OSHA has subsequently proposed (59 FR 28594, June 2, 1994) to revise its marine terminal (part 1917) and longshoring (part 1918) standards. Those proposed standards (proposed §§ 1910.16(b)(2), 1917.1(b)(2)(xiv), and 1918.1(b)(1)) would apply OSHA's toxic substance standards (part 1910, subpart Z) only when the packaging in which a substance is being transported in the maritime environment has broken open. This language, based on the existing marine terminal standard (§ 1910.16(b)(2)(ii)), reflects the view that hazardous substances, when properly packaged, do not pose significant exposure risks for the shipyard employees transporting them in closed packages.

Therefore, as revised, final rule §1910.19(m) states that §1910.1052 will address MC exposure in marine terminal and longshore employment only where leaking or broken packages allow MC exposure that is not addressed through compliance with 29 CFR parts 1917 and 1918. Given the promulgation of § 1910.19(m), the Agency has determined that it is unnecessary to mention marine terminals and longshoring in final rule § 1910.1052(a), *Scope and application*.

OSHA has not learned of any circumstances in which marine terminal or longshore employees have been exposed to MC because of damage to packaging. The Agency, accordingly, anticipates that the MC final rule will have little or no impact on the marine terminal and longshoring industries.

In developing this rule, OSHA has consulted with its Shipyard Employment Standards Advisory Committee (SESAC) to obtain information on MC use and exposure in shipyards and has taken the Committee's input into consideration in developing the standard. In particular, OSHA has relied on data provided by SESAC in assessing the technological feasibility and costs of compliance of the standard for shipyards covered by the rule.

Since the construction industry is also included in the scope of the final rule, OSHA is required to consult the Advisory Committee on Construction Safety and Health (ACCSH) in accordance with section 107 of the Contract Work Hours and Safety Standards Act (40 U.S.C. 333) (the Construction Safety Act) and 29 CFR 1911.10. On July 28, 1992, OSHA formally consulted with ACCSH regarding the construction-specific aspects of occupational exposure to MC. The Agency solicited comment and testimony regarding ACCSH's recommendations through a Federal Register notice (57 FR 36964, August 17, 1992). One of ACCSH's suggestions was that the rule specifically require originators of contract bids to stipulate a requirement for compliance with the MC standard in their bids. OSHA has not adopted this suggestion in the final rule because construction contracts already require compliance with all relevant Federal regulations. The specific suggestions made by ACCSH and OSHA's responses to ACCSH's input are discussed below in the relevant paragraphs of the Summary and Explanation.

In the proposal, the scope and application paragraph included an exemption for employers with workplaces where MC products were present but objective data were available to demonstrate that the product could not release MC above the action level or STEL under those foreseeable conditions of processing, use, and handling that would cause the greatest possible release. This concept remains in the final standard, although the provision has been moved to the

exposure monitoring section (paragraph (d)), because this provision constitutes, in effect, an exception to the standard's requirement for initial monitoring.

The Air Transport Association [Ex. 19–75] requested that airlines be excluded from the general industry standard, and that a separate standard covering MC use in the airline industry be developed. OSHA has specifically determined that the exposures, work operations, and means of compliance for aircraft-related MC uses are similar to those in many other establishments and thus that there is no substantive basis for the requested exemption. Consequently, OSHA has concluded that no industry-specific standard for airlines is warranted. MC uses in the airline industry are discussed in the section of the final economic analysis entitled ''Aircraft Stripping.''

Paragraph (b) Definitions

This paragraph includes definitions of a number of terms used in the regulatory text of the final standard. Although some of these terms are in common use, OSHA believes that these definitions will help to ensure that their meaning in the context of the standard is clear.

Action level means an airborne concentration of MC of 12.5 ppm, measured as an 8-hour time-weighted average. One purpose of the action level is to relieve the burden on employers by providing a cut-off point below which many of the compliance activities in the standard are not required. In addition, due to the variable nature of employee exposures to airborne concentrations of MC, compliance with an action level provides employers with greater assurance that their employees will not be exposed to MC concentrations above the permissible exposure limits.

The action level also increases the cost-effectiveness and performance orientation of the standard while improving employee protection. The standard will encourage employers who can, in a cost-effective manner, identify approaches or innovative methodologies to reduce their employees' exposures to levels below the action level, because this will eliminate the costs associated with exposure monitoring and medical surveillance, two provisions of the standard that are triggered by exposure exceeding the action level. At the same time, the employees of such employers will be protected because their MC exposures will be less than half of those permitted by the permissible exposure limit. Employees of those employers who are not able to lower exposures below the action level will have the additional protection provided by medical surveillance, exposure monitoring, and the other provisions of the standard that are triggered by the action level.

The statistical basis for using an ''action level'' has been discussed in connection with several other OSHA health standards [see, for example, acrylonitrile (29 CFR 1910.1045) and ethylene oxide (29 CFR 1910.1047)]. In brief, although all employee exposure measurements on a given day may fall below the permissible exposure limit, some probability exists that on unmeasured days the employee's actual exposure may exceed the permissible exposure limit. Where exposure measurements are above the action level, the employer cannot reasonably be confident that the employee may not be overexposed on a given day. Therefore, requiring periodic employee exposure measurements to begin at the action level provides the employer with a reasonable degree of confidence in the results of his or her exposure measurement program [Ex. 7–248]. OSHA's decision to set the action level at one-half the PEL is based on its successful experience using this fraction as the action level in many standards, such as arsenic, ethylene oxide, vinyl chloride and benzene.

OSHA received comments from a number of rulemaking participants [Exs. 19–16, 19–20, 19–22, 19–31, 19–47, 19–75] suggesting that the proposed PELs and, by association, the action level, be revised. For instance, Hukill Chemical Corporation [Ex. 19–47] argued that the action level should be set at 100 ppm because it believes that: 1) CNS effects from MC are not observed in humans until 300 ppm; and 2) there is no evidence of excess cancer mortality in humans up to a level of 475 ppm. As explained in the Health Effects and Quantitative Risk Assessment sections of this preamble, OSHA disagrees with this commenter because the Agency has determined that significant risks exist at levels substantially below those referred to by the commenter and therefore that the suggested levels would not be adequately protective.

The Pharmaceutical Manufacturers Association (PMA) [Ex. 19–25] commented that the action level of 12.5 ppm is appropriate, but requested an exemption from ''various requirements of the standard'' if exposure occurs on fewer than 30 days a year. In particular, PMA suggested that periodic monitoring be required only when there is exposure above the PEL or STEL for at least 10 days a year or at or above the action level for at least 30 days a year. OSHA has considered this issue, along with similar concerns raised by ACCSH, and agreed that in cases where exposure occurs only on a few days per year, it was appropriate to alter the exposure monitoring requirements. Specifically, paragraph (d)(2)(iii) would permit employers whose employees are exposed to MC on fewer than 30 days per year to forego the initial monitoring required by paragraph (d)(2), provided that the employer has taken measurements that give immediate results (such as those taken by detector tube) and that provide sufficient information about exposures to determine what (if any) control measures are necessary. In addition, the medical surveillance requirement (paragraph (j)), with the exceptions described in the final rule, applies only where employees are exposed above the action level on at least 30 days within a year or above the PELs on at least 10 days within a year.

Newport News Shipbuilding [Ex. 19–37] suggested that the action level be set at 15 ppm. However, adopting this suggestion would not be consistent with the statistical basis for establishing the action level at one-half the PEL, as described above. In addition, Markey Restoration Company [Tr. 2671–72, 10/16/92] recommended that the action level be eliminated based on the costs of medical surveillance triggered by that level. As noted above, an action level is based on the probability of exceeding the PEL and is designed to enhance both employee protection and the standard's cost-effectiveness, and OSHA does not believe it would serve either employers or employees to eliminate this concept from the final rule.

The UAW [Tr. 1885–86, 9/24/92] questioned the statistical arguments underpinning the action level that OSHA has used for some years. According to the UAW's calculations, the action level should actually be set at one-tenth the PEL to accomplish the purpose OSHA intended. Accordingly, the UAW argued that: ''[I]f you leave it [the action level] at 1/2, [there is] almost the virtual certainty that workers are overexposed on that job.'' In response, OSHA notes that its experience with action levels set at one-half the 8-hour TWA PEL has been favorable and that employers and employees have benefitted from the use of the action level concept. In particular, it is OSHA's experience that, for most workplaces, variability is normally such that an action level set at one-half the TWA PEL is appropriate. The final standard thus continues this practice.

Emergency means any occurrence, such as but not limited to, equipment failure, rupture of containers, or failure of control equipment, which results, or is likely to result in an uncontrolled

release of MC. The word ''uncontrolled'' was changed from ''unexpected'' in the proposal to be more descriptive and to be consistent with the Hazard Communication Standard (29 CFR 1910.1200) and the Hazardous Waste Operations and Emergency Response Standard (29 CFR 1910.120). Incidental releases of MC—i.e., those where the substance can be absorbed, neutralized, or otherwise controlled at the time of release by maintenance personnel or other employees working in the immediate release area—are not considered to be emergencies within the scope of this standard. Dow Chemical Company [Ex. 19–31] indicated that the examples of emergencies provided in the proposal (purging lines and cleaning sludge from tanks) should not be included in the final rule. Other commenters [Exs. 19–25, 19–28, 19–57] agreed with Dow that the examples provided with the definition in the proposal were inappropriate. In particular, Eli Lilly and Company [Ex. 19–28, p. 7] stated

> Lilly agrees with the concept that an emergency should be tied to unexpected releases. It is therefore curious and illogical that the examples given—purging of lines and cleaning tanks—are not unexpected events. To the contrary, in the pharmaceutical industry these are planned events which could even occur daily.

On the other hand, the Upjohn Company [Ex. 19–49] commented as follows:

> The language ''unexpected significant release'' is very vague and will not result in any consistent interpretation as to what type of a release meets this definition. We would recommend that the language be changed to ''* * * which may lead to employee exposure at or above the eight hour, timed-weighted average (TWA) or at or above the short-term exposure limit (STEL).''

OSHA acknowledges that the language in question could be misunderstood and has deleted the parenthetical listing of some examples of emergency situations. Furthermore, the Agency recognizes that emergency situations, by their very nature, are difficult to anticipate and describe. Therefore, OSHA has not provided examples of emergency situations in the final rule. Instead, the final rule lists situations that OSHA does not consider emergencies, because these will help employers to identify situations in their workplaces that do constitute emergencies. OSHA recognizes that emergencies have certain aspects in common but that other aspects are specific to a given workplace. For example, employee exposure must be uncontrolled for an emergency to exist. Provisions of the standard that include requirements that employers must meet in case of an emergency include Methods of Compliance, Respiratory Protection, Medical Surveillance, and Employee Information and Training.

Employee exposure is defined as that exposure to airborne MC which occurs or which would occur if the employee were not using respiratory protective equipment. This definition is consistent with OSHA's previous use of the term ''employee exposure'' in other health standards.

Methylene chloride (MC), or dichloromethane, means an organic compound with the chemical formula, CH2Cl2. Its Chemical Abstracts Registry Number is 75–09–2. Its molecular weight is 84.9 g/mole. Other information regarding the characteristics of MC may be found in the appendices to the final standard. MC is a colorless, volatile, liquid with a chloroform-like odor and is not flammable by standard tests in air, but will burn under extreme conditions. It has a boiling point of 39.85 C (104 F) at standard atmospheric pressure, a lower explosive limit of 12% and an upper explosive limit of 19.5% in air. It is completely miscible with most organic solvents but is sparingly soluble in water (1.3% by weight at room temperature). It has an extensive oil and fat solubility. Decomposition products during combustion or fire include phosgene, hydrochloric acid and carbon monoxide.

Physician or other licensed health care professional is defined as a person whose legally permitted scope of practice allows him or her to independently provide or be delegated the responsibility to provide some or all of the health care services required by final rule paragraph (j), Medical Surveillance. Use of this phrase is designed to increase the flexibility of the standard; the proposal used the more restrictive term ''physician.'' OSHA intends that employers should consider the opinion of the applicable state licensing board, which defines the scope of practice for licensed health care professionals, when they are determining the appropriate provider to supply some or all of the medical services required by the standard. The new terminology recognizes that there are many services that non-physicians can provide, that some non-physicians have particular expertise in diagnosing and treating occupationally related diseases, and that the use of these providers is often a cost-effective and protective approach to the provision of medical care.

Regulated area means an area, demarcated by the employer, where an employee's exposure to airborne concentrations of MC exceeds or can reasonably be expected to exceed either the eight (8)-hour time-weighted average limit or the short-term exposure limit. The wording of this definition has been changed slightly from that in the proposal for clarity. The requirements for regulated areas are discussed below in relation to paragraph (e).

OSHA has added a definition for *symptom* to the final rule to clarify what is meant by that term when it is referred to in the regulatory text. MC has a wide range of possible adverse health effects. This definition clarifies what portion of that range would be considered a symptom for purposes of the standard. The covered symptoms would include indications of central nervous system effects, such as headaches, disorientation, dizziness, fatigue, and decreased attention span; cardiac effects, such as chest pain and shortness of breath; and skin effects, such as chapping, erythema, or skin burns.

The definitions of ''*Assistant Secretary*,'' ''*Authorized Person*,'' ''*Director*'' and ''*This section*'' are consistent with OSHA's previous uses of these terms in other health standards.

The Boeing Company [Ex. 19–26] suggested that a definition be added for ''*work area*'' to preclude unnecessary monitoring in areas that do not contain MC. OSHA does not believe that this is necessary. If there is no MC present in an area, no monitoring needs to be performed for MC. In addition, the focus of this standard is employee exposure, as measured by personal monitoring, and not particular locations.

Paragraph (c) Permissible Exposure Limits

OSHA is promulgating an 8-hour time-weighted average (TWA) permissible exposure limit (PEL) of 25 ppm, and a short-term exposure limit (STEL) of 125 ppm averaged over 15 minutes, as proposed. OSHA has determined, based on evidence in the record, that occupational exposure to MC at the current 500 ppm 8-hour TWA PEL presents a significant risk of material health impairment, and particularly of cancer, to exposed employees and that compliance with the new standard will substantially reduce that risk. In combination with the STEL, the 8-hour TWA PEL and the other industrial hygiene provisions of the standard will also protect exposed employees from the other health effects caused by exposure to MC.

The basis for the 8-hour permissible exposure limit is discussed above in the sections on Health Effects and Significance of Risk, as well as in the economic analysis. OSHA believes that

compliance with the new 25 ppm 8-hour TWA PEL is feasible and necessary to protect exposed employees from this significant risk of material health impairment.

OSHA received comments from a number of rulemaking participants suggesting that the proposed PELs and, by association, the action level be revised. The arguments for revising the proposed PELs were based on interpretations of the scientific support for given PELs and the feasibility of particular PELs in certain situations. Some commenters felt that the current level of 500 ppm does not provide adequate protection for employees and agreed that the PEL should be set at 25 ppm [Exs. 19–15, 19–49]. Specifically, Striptech International, Inc. [Ex. 19–15] stated:

> The OSHA proposed 25 ppm standard for MC does substantially eliminate significant risk and it is feasible and definitely appropriate. The technology exists to enable the industries using MC to comply or to use an alternate method.

However, a number of rulemaking participants [Exs. 19–22, 19–23, 19–36, 19–38, Tr. 530, 9/18/92, Tr. 1776, 9/24/92, Tr. 1869, 9/24/92] suggested that OSHA set the 8-hour TWA PEL below 25 ppm, because they believe that the proposed 25 ppm limit would not adequately protect workers. For example, the UAW stated that setting a PEL at 25 ppm ''will permit too much exposure to methylene chloride, therefore placing workers at great risk, contrary to the requirements of the OSHA Act'' [Tr. 1869, 9/24/92]. The UAW stated that the proposed limit ''would permit 2 deaths per thousand workers,'' and therefore suggested setting a PEL of 10 ppm, which the union felt would be feasible through specified engineering and work practice controls [Ex. 19–22, Tr. 1869, 9/24/92]. Scott Schneider, representing the IUE, also suggested that ''because of the evidence of health effects from low level exposures'' to MC, the PEL should be lowered below 25 ppm [Ex. 19–38]. The IUE and the ACTWU both supported the UAW recommendation of 10 ppm [Tr. 530, 9/18/92, Tr. 1776, 9/24/92].

The Laborers' Safety and Health Fund of North America [Ex. 19–36] suggested that worker exposure should be controlled to the lowest feasible level, which is consistent with NIOSH's position. NIOSH recommended ''that occupational exposure to methylene chloride, which is a potential occupational carcinogen and may induce ischemic heart disease, be reduced below the proposed PEL to the lowest feasible level'' [Tr. 868, 9/21/94]. OSHA agrees with these commenters that a significant risk remains at 25 ppm, but believes that this level is the lowest level for which OSHA can currently document feasibility across the affected application groups and industries.

OSHA's primary justification for the new standard is the risk of cancer associated with exposure to MC. Some commenters stated that the carcinogenicity of MC has not been proven and therefore that carcinogenicity should not be the basis for setting the PEL [Exs. 19–18, 19–29, 19–31, 19–45]. In particular, Kodak [Ex. 19–18] stated that it ''does not believe that the human or animal data demonstrate a need to establish methylene chloride exposure limits at the levels proposed by OSHA in order to adequately protect employee health.'' Mr. Bixenman, representing Benco Sales, testified [Tr. 2638, 10/16/92] ''And surely with our current level of technology, if methylene chloride were a human carcinogen, it could be established without question with actual diagnosed cases.'' Also, the Air Transport Association stated [Ex. 19–75]:

> [T]he limited findings regarding cancer in mice at high MC dosage is weak justification for the proposed regulatory action. None of our members have found permanent health symptoms related to the use of MC, while usage at some facilities goes back at least 30 years. We have no data or experience connecting heart disease with MC use.

As discussed more extensively in the Quantitative Risk Assessment section, above, OSHA has based its assessment of MC cancer risk on the determination (supported by the NTP, EPA, and other agencies) that there is clear evidence of MC carcinogenicity in mice and rats. Although there are a few substances for which clear evidence of carcinogenicity in rodents has been deemed to be irrelevant to humans due to compelling evidence of mechanisms of action unique to the species tested, no such evidence exists for MC. In fact, as discussed in the Risk Assessment section, mechanistic evidence adds to the weight-of-the-evidence suggesting that MC is also carcinogenic in humans.

OSHA's final risk estimate indicates a risk of 7.5 deaths per 1000 workers exposed to MC at 50 ppm over a working lifetime and a risk of 3.6 deaths per thousand workers exposed to MC at 25 ppm over a working lifetime. OSHA has determined, using quantitative risk assessment, that the estimated risk of developing cancer warrants setting the 8-hour TWA PEL at 25 ppm and a 15-minute STEL at 125 ppm; in fact, at the 25 ppm PEL the residual risk still greatly exceeds any significant risk threshold, and only the lack of documentation of the feasibility of lower PELs across the affected industries has convinced the Agency not to reduce the PEL even further at this time.

OSHA disputes the contention of Mr. Bixenman that ''actual diagnosed cases'' are a precondition for establishing that a particular substance is carcinogenic to humans. Due to the natural background rate of all cancers, epidemiologic studies of groups are the only way to analyze human cause-effect relationships. As discussed in the Quantitative Risk Assessment section, OSHA has concluded that some of the available epidemiologic studies suggest a positive association between MC exposure and human cancer and that no epidemiologic studies of sufficient power exist to cast serious doubt on such conclusions.

Several commenters preferred a PEL of 50 ppm, which is the current ACGIH threshold limit value for MC, because they felt that a 25 ppm PEL would be either too costly to implement or the technology to achieve such a level of control was not available [Exs. 19–2, 19–3, 19–12, 19–14, 19–15, 19–29, 19–31, 19–35, 19–37, 19–39, 19–48, 19–50, 19–56, 19–57]. For example, Abbott Laboratories [Ex. 19–29] commented that specific processes in the pharmaceutical industry ''cannot be controlled through existing conventional engineering controls.'' Also, AMETEK [Ex. 19–12] stated that ''It will be hard for many industries to reach the 50 ppm level and extremely difficult, if not, impossible, for most to reach the 25 ppm level.'' Therefore, this commenter proposed ''that OSHA set the PEL for methylene chloride at 50 ppm (8-hour TWA) with no AL [action level] and leave the STEL at 125 ppm (15-minute average) as originally written.'' AMETEK contended that this approach ''combines aspects of both ACGIH guidelines and OSHA's proposed standard into a regulation which would be both protective of worker health and economically feasible for industry'' [Ex 19–12].

Many other commenters argued for a PEL of at least 100 ppm [Exs. 19–1, 19–4, 19–10, 19–11, 19–16, 19–24, 19–47, 19–51, 19–52, 19–53, 19–54, 19–67, 19–75, 19–79, 98, 115–3, Tr. 397, 9/17/92, Tr. 2216, 10/14/92, Tr. 2627, 10/16/92, Tr. 2671, 10/16/92, Tr. 2702, 10/16/92]. For example, Besway Systems, Inc., testified [Tr. 397, 9/17/92]: ''We would like to see a PEL for these companies of 200 ppm, which we've been able to show is safe and economically attainable in our real life experience. We

believe that the absolute maximum PEL for our industry should be set at 100 ppm eight hour time weighted average. . . .'' Also, Benco Sales [Tr. 2627, 10/16/92] stated ''We feel the American workers would receive more benefit by implementation of an exposure level of 100 parts per million, which is achievable, and the subsequent enforcement of that level.'' ChemDesign Corporation [Ex. 19–24] believes that the ''sharp reduction in the exposure limit is unjustified based on lack of credible data that this chemical has the potential to cause cancer in humans.'' This commenter therefore suggested that the PEL be ''lowered by a factor of five to 100 parts per million'' [Ex. 19–24].

Other commenters supported a variety of PEL values. One suggested that a lower PEL be phased in over time, with 75 ppm for two years, then 50 ppm for two years, and finally 30 ppm [Ex. 19–20]. The reasoning behind this suggestion was that, during this period, alternative options to best fit specific operations could be evaluated and implemented and sufficient time provided to gather the funds necessary to implement the entire system [Ex. 19–20]. OSHA holds, however, that the types of engineering controls required under this standard are relatively simple and that engineering to 75 ppm, then 50 ppm, then 30 ppm is likely to be more costly in time and money than engineering to or below 25 ppm initially. The suggested phase-in would also be administratively burdensome for employers, who would be subject to changing OSHA requirements over the years, with no clear advantage in reducing the costs of compliance. In addition, if OSHA allowed such a phase-in period, workers would be exposed to MC at higher levels than would occur if OSHA required no phase-in period. Therefore, the Agency sees no advantage to using the phased-in approach described. Moreover, the Agency notes that the time-frames for compliance with the provisions of the standard, including implementation of engineering controls, have been tailored to the size of the establishments, in order to give all employers a reasonable amount of time to gather resources and information necessary to comply with this regulation. See the discussion of start-up dates later in this document.

Smith Fiberglass Products, Inc. suggested that the PEL should remain at 500 ppm because there is no evidence of human harm at the present PEL and STEL, since ''studies with rats and mice show that only a serious overdose far above the present STEL can cause carcinogenic effects'' [Ex. 19–82]. Another commenter [Ex. 19–86] stated that ''The present PEL of 500 parts per million (ppm) is not protective enough of employees based on toxicological data developed since the PEL was established.'' This commenter therefore suggested that the PEL should be lower than 500 ppm but higher than 25 ppm (no specific value identified). As discussed above, however, OSHA has determined that exposure to MC above 25 ppm poses significant cancer risks and that it is feasible to protect affected employees from those risks (see the Significance of Risk section of the preamble).

A number of commenters addressed the availability of suitable substitutes for MC in their concerns about feasibility [see, e.g., Exs. 19–6, 19–8, 19–37, 19–43, 19–55, 19–74, 19–79, 19–84, 115–3; Tr. 433, 9/17/92; Tr. 1591, 9/23/92; Tr. 1712–13, 9/24/92; Tr. 2636–38, 10/16/92]. Substitution is often a valid means of controlling exposures to a particular hazardous chemical when a less hazardous substitute is available that can be used to perform a similar function. In particular, some commenters stated that there are no viable substitutes for MC products used to perform particular tasks. These participants argued that companies would go out of business because they would be unable to comply with the final standard in a feasible way [Exs. 19–6 and 19–8]. In addition, one commenter [Ex. 19–8] expressed concern that substitute products would pose fire hazards. The National Tank Truck Carriers, Inc. testified [Tr. 1712, 9/24/92]:

> One company which discontinued the use of methylene chloride found it necessary to supplement the methylene chloride substitute with even more hazardous acetone and toluene in order to remove the residues from the trailers and containers and properly service the industry by providing clean trailers.

OSHA has determined that for all application groups, compliance with this regulation can generally be achieved through the use of engineering controls and work practices. The Agency's Final Economic Analysis estimated the cost of compliance assuming that almost all firms would continue using MC and that only a small fraction of firms would substitute away from MC. OSHA agrees that, in an individual establishment, the potential use of substitution as a means of control must be evaluated carefully to ensure that the magnitude of the hazard posed is not the same or increased as a result of the substitution. For some applications described in this regulation, many substitutes for MC are available for specific applications that do not pose increased health or safety hazards. In general, however, OSHA has based it findings of feasibility not on the ability of companies in the affected sectors to substitute away from MC but on their ability to implement conventional engineering and work practice controls.

In addition to the 8-hour TWA PEL, OSHA is promulgating a short-term exposure limit (STEL) of 125 ppm, measured over a 15-minute period, to protect employees from the acute toxicity of MC and its metabolites. The acute toxicity of MC is characterized primarily by CNS effects, such as decreased alertness and coordination, headaches, and dizziness, which may lead, in turn, to accidents on the job as well as material impairment of health. Absence of a STEL would mean that employees could be exposed to up to 800 ppm for 15 minutes. Such levels are clearly associated with central nervous system effects.

MC is also metabolized to carbon monoxide (CO). CO produced from MC exposure has the same toxic effects in the body as direct exposure to CO does. The primary toxic effect of CO is reduction of the ability of the blood to carry oxygen to the tissues of the body.

In the body, carbon monoxide is converted to carboxyhemoglobin. Background levels of carboxyhemoglobin in the non-smoking U.S. population vary from approximately 0.5% to 2.0%. Carboxyhemoglobin in smokers ranges from approximately 3% to 10%. Additional body burden of CO (carboxyhemoglobin) due to MC or direct CO exposure can have adverse health effects on affected individuals. For example, exposure to relatively low levels of carbon monoxide (for example, levels which increase carboxyhemoglobin by 2%) reduced time to angina in patients with pre-existing heart disease exposed to occupational levels of CO [Ex. 21–93]. Exposure of pregnant women to CO has been shown to produce adverse health effects on the developing fetus. Workers with anemia or other blood abnormalities may be at increased risk of material impairment to health because of an already decreased oxygen-carrying capacity.

The carbon monoxide-mediated cardiac effects of MC exposure are of particular concern in the occupational setting because a significant fraction of the U.S. working population (some investigators estimate 30% of the U.S. population) has silent or symptomatic heart disease. NIOSH has expressed concern that the STEL proposed by OSHA is not low enough to protect

workers from the adverse central nervous system and cardiac effects of MC.

In addition to reducing risks of cardiac and CNS effects, the STEL will also enhance employee protection from MC-induced carcinogenesis by reducing total exposure to MC and by limiting the metabolism of MC by the GST pathway (the putative carcinogenic metabolic process). Metabolic evidence suggests that the GST pathway produces more than proportionately greater quantities of the putative carcinogenic metabolite when MC concentrations reach levels of about 100 ppm. For this reason, it is important to limit high concentration, short duration exposures to MC. Thus the STEL will reduce the exposure-related risks of acute CNS effects, episodes of carboxyhemoglobinemia, and cancer.

Another advantage in requiring a STEL is that it focuses attention on sources of MC exposure in the workplace. General industrial hygiene principles state that a well-controlled process should have peaks no higher than five times the 8-hour TWA. Measurement of STEL exposures can indicate point sources which have unacceptably high MC emissions and help the employer target those processes for abatement. This can be an efficient mechanism to concentrate industrial hygiene resources on those emission sources which, when controlled, will reduce total employee MC exposure.

In addition, it has been established that ''[i]f in fact a STEL would further reduce a significant health risk and is feasible to implement, then the OSH Act [section 6(b)(5)] *compels* the agency to adopt it barring alternative avenues to the same result.'' (emphasis in the original) *Public Citizen Health Research Group* v. *Tyson*, 796 F.2d 1479, 1505 (D.C. Cir. 1986) (Ethylene oxide). See also *Building and Construction Trades Department, AFL–CIO* v. *Brock*, 838 F.2d 1258, 1271 (D.C. Cir. 1988) (Asbestos).

In summary, many commenters questioned the need for a reduced PEL, for a PEL of 25 ppm, and for the particular 8-hour TWA PEL-STEL combination proposed by OSHA, citing concerns about the feasibility of these limits and the ability of companies to identify controls and/or substitutes to comply with them. However, as discussed in the final economic analysis, OSHA has determined that it is both technologically and economically feasible for facilities in all affected sectors to comply with the final rule. In almost every case, companies will be able to use conventional engineering controls and work practices to reduce their employees'' exposures to these levels. In addition, many employers will find that substitution is a viable approach to eliminating the significant risk posed to workers by MC. As the economic analysis points out, many firms in many of the covered industries have already substituted away from MC, and have enjoyed considerable cost savings in the process. Finally, it is important not to lose sight of the reasons for regulating MC in the first place: this substance poses a significant risk of cancer, central nervous system and cardiac effects, and sensory irritation to the quarter of a million workers who manufacture, formulate, use, or transport this substance in the workplace.

As the Quantitative Risk Assessment and Significance of Risk sections of the preamble demonstrate, the cancer risk remaining at an 8-hour TWA PEL of 25 ppm is clearly of great concern, in that it exceeds the 1/1000 level indicated by the Supreme Court to be clearly significant. OSHA therefore encourages employers to further reduce the MC exposures of their employees wherever it is feasible to do so. Because the residual risk remaining at 25 ppm is great, the Agency intends to gather data and information on the feasibility of reducing the 8-hour TWA PEL to reduce remaining significant risk in a future rulemaking action. The priority assigned to any future rulemaking activity will depend in large measure on the prevailing exposure levels, feasibility, scientific advances and other information, at the time OSHA considers further proposals; to the extent prevailing levels are significantly below 25 ppm, the need for subsequent proposals will diminish.

Paragraph (d) Exposure Monitoring

Paragraph (d) addresses the employee exposure monitoring requirements for workplaces where employees are exposed to MC. As discussed in the preamble to the proposed rule (57 FR 57118–20), OSHA requires employee monitoring to facilitate compliance with the PELs. As a general matter, exposure monitoring of employee exposure to toxic substances is a well-recognized and accepted risk management tool. The monitoring provisions of this final MC standard are consistent with the monitoring provisions of other OSHA standards. Section 6(b)(7) of the OSH Act, which addresses rulemaking requirements for hazardous chemicals, requires health standards to include provisions for monitoring employee exposures. In the final rule, the exposure monitoring provisions have been reorganized and rewritten to improve their clarity and readability. The substance of the requirements is essentially the same, with the few exceptions noted below.

The provisions of proposed paragraph (d) elicited a considerable amount of comment and testimony. Several rulemaking participants [Ex. 19–57; Tr. 249, 9/17/92; Tr. 458, 9/17/92; Tr. 1711, 9/24/92] stated that the proposed requirements for exposure monitoring would impose excessive economic burdens on some employers (e.g., paint strippers, tank cleaners). However, in the final rule OSHA has structured the exposure monitoring requirements to minimize the burden for employers whose employees have lower exposures and for workplaces where groups of employees have similar exposures. In addition, the Agency has included some alternatives to the initial monitoring provisions that will reduce the amount of monitoring required for some workplaces. Ultimately, however, the Agency has determined that it is essential to the protection of exposed employees that exposure levels be quantified in order to select and implement the proper measures to reduce employee exposures to MC.

The overall rulemaking record supports the need for exposure monitoring to ascertain exposure levels for the purpose of designing appropriate protective measures for employees. In addition, evidence in the record indicates that the exposure monitoring requirements are economically and technologically feasible for firms in all of the affected industry sectors. (See the discussion in the Final Economic Analysis [Ex. 129].)

Paragraph (d)(1) sets forth the general requirements that apply to all monitoring provisions. Paragraph (d)(1)(i) states that employers must characterize the MC exposure of each employee. Employers may chose one of two ways to determine an employee's MC exposure level. First, the employer can take a personal air sample in the breathing zone of each affected employee. This approach is the most precise method of exposure monitoring because it allows each employee's exposure to be individually ascertained. However, OSHA recognizes that this approach may be burdensome for employers with many employees. Therefore, paragraph (d)(1)(ii) permits employers to establish a representative monitoring scheme.

Under this option, a personal breathing zone air sample may be considered representative of another employee's 8-hour TWA or STEL exposure if the following conditions are met. First, the sampled employee must

be that employee who is likely to have the highest MC exposure among the employees included in the group that is to be represented by the sample. Second, if the employer wishes a sample taken on an employee in a given job on one work shift to represent the exposure of another employee in the same job classification on another shift, the employer must sample at least one employee in each job classification in each work area during every work shift. Paragraph (d)(1)(ii) also contains an exception under which a personal breathing zone sample taken on one employee in one job classification in a given work area and on a particular shift will be considered representative of the exposure of employees on other shifts, where the employer documents that the tasks performed and conditions in the workplace are similar for all employees whose exposures are represented.

The provision for representative sampling, which is very similar to the corresponding provision of the proposed rule, eliminates unnecessary monitoring and thus further improves the cost-effectiveness of the standard. In a change from the proposal, the final standard also allows employers to use representative monitoring to comply with the standard's requirement for initial monitoring. OSHA believes that representative initial monitoring is appropriate in those cases where the employer can accurately determine which employees are likely to have similar exposures.

The accuracy of the methods used to perform exposure monitoring is addressed under paragraph (d)(1)(iii). For monitoring of airborne concentrations above the 8-hour TWA PEL or the STEL, the results must be accurate within plus or minus 25 percent at a confidence level of 95 percent. Where concentrations are above the action level but at or below the PEL, the accuracy must be within plus or minus 35 percent at a confidence level of 95 percent.

Methods of measurement are presently available that can detect MC within these limits. One such method is OSHA method 80, which has a limit of detection of 0.201 ppm. Copies of this method are available from OSHA and can be downloaded from OSHA's World Wide Web site on the Internet at ''http.www.osha.gov/.'' Sampling and analysis may also be performed by portable direct reading instruments, real-time continuous monitoring systems, passive dosimeters or other methods that meet the accuracy and precision requirements of the standard under the particular conditions which exist at the employer's worksite.

Paragraph (d)(2) requires employers to make an initial determination of affected employees' exposure to MC. OSHA anticipates that most employers will need to perform monitoring in order to characterize employee exposure and has framed the rule accordingly. The standard allows employers to characterize their employee exposures using other means, providing that they can meet the requirements for such other means presented in the standard. For example, as discussed above, some employers may have objective data that establishes that employees will not be exposed above the action level or the STEL under reasonably foreseeable circumstances. Some employers generate such data themselves, while others rely on information provided by the manufacturer or supplier. Accordingly, paragraph (d)(2)(i) provides that employers can rely on objective data in certain circumstances in lieu of performing initial monitoring. The objective data must represent the highest MC exposures likely to occur under reasonably foreseeable conditions of proccessing, use, or handling in the workplace, and the employer must document the objective data relied on (see paragraph (m)). This provision corresponds to proposed paragraph (a)(2), which was the subject of several comments [Exs. 19–14. 19–31, 19–57].

Occidental Chemical testified [Tr. 2010 and 2023, 10/14/92] that OSHA should expand the proposed objective data exemption so that mixtures with less than one percent MC would be excluded from the scope of the MC standard. The Hazard Communication Standard (HCS) addresses mixture composition for the purpose of identifying those constituents and concentrations that impart their hazardous characteristics to the mixture as a whole. According to the HCS, carcinogenic substances such as MC are considered to impart their carcinogenic characteristics to the mixture if they are present in concentrations of more than one-tenth of one percent or can be released in concentrations that exceed an existing PEL. This is a much more protective requirement than that suggested by Occidental, and the Agency believes it would be inappropriate to lessen the protections provided to employees under the HCS in this substance-specific MC standard. Therefore, OSHA has not made the suggested change.

In addition, OSHA recognizes that it would be unreasonable to require initial monitoring under this standard where employers have already performed the monitoring needed to characterize employee exposure. Paragraph (d)(2)(ii) allows employers who have monitored their employees' exposures to MC within one year prior to April 10, 1997 and that monitoring complies with the accuracy and other requirements for monitoring contained in the final rule, to designate such monitoring results as sufficient in lieu of performing the initial monitoring.

Dow Chemical Co. [Ex. 19–31] commented that OSHA should allow monitoring data collected as much as two years prior to the effective date of the final rule to qualify as initial monitoring data. The Agency believes that data more than a year old would be unlikely to provide a reliable basis for characterizing employee exposure, because workplace conditions may well have changed since such data were collected. Accordingly, the Agency has not made the suggested change.

Addressing this point, Scott Schneider of the International Union of Electronic, Electrical, Salaried, Machine and Furniture Workers (IUE) testified [Tr. 531, 9/18/92] as follows:

> While we support the requirements for exposure monitoring that were proposed, we have reservations about section (d)(2)(ii) regarding the use of ''earlier monitoring results'' to satisfy the initial monitoring requirements. OSHA must specify exactly which requirements the data must meet, in terms of both quality and quantity. Otherwise, it will be an enormous loophole for companies to avoid monitoring.

The International Brotherhood of Painters & Allied Trades (IBPAT) agreed with Mr. Schneider; the union stated that the use of ''historical monitoring data to characterize exposures for similar processes * * * may lead to erroneous estimates of actual exposures'' [Ex. 19–23]. OSHA believes that the concerns of these commenters have been addressed in the final rule because, to be acceptable under the standard, any previously gathered exposure data must meet the analytical, sampling, and other requirements specified for initial monitoring.

A number of commenters addressed the application of monitoring requirements in construction [Ex. 19–23; Tr. 544–45, 9/18/92; Tr. 814–17, 9/21/92; and Tr. 1377–80, 9/23/92]. OSHA agrees that conditions on construction sites often present special industrial hygiene and monitoring problems, particularly since the job may be completed before sampling results taken by conventional personal monitoring methods have been returned from the laboratory. For example, IBPAT [Ex. 19–23] pointed to the exposure variability that typifies construction sites, noting that weather, a highly transient workforce, and other factors often

complicate accurate characterization of construction worker exposures. OSHA's Advisory Committee for Construction Safety and Health (ACCSH) and other participants suggested that OSHA allow the use of direct-reading instruments to address this problem [ACCSH Tr. 100–103, 7/28/92; Workgroup report, pp. 3–4; Tr. 814–818, 9/21/92; Tr. 1377–1382, 9/23/92].

In response to these comments, the final rule has been revised to allow the use of such instruments where employees are exposed to MC on fewer than 30 days within a given year. This means that construction employers who are involved in short-term construction projects will be able to use these instruments to characterize the MC exposures of their employees. Paragraph (d)(2)(iii), which addresses transient workplaces or work operations where employees are exposed on fewer than 30 days a year, permits employers to use direct reading instruments such as detector tubes to estimate exposure and determine what protective measures to provide to their MC-exposed employees. Although these simple measurement tools often do not meet the accuracy requirements that other types of monitoring methods do, they have the advantage of immediate results and thus allow employers to provide protection immediately. OSHA believes that this provision is responsive to the comments discussed above and represents an effective solution to a difficult worker protection problem.

Paragraph (d)(3) addresses periodic monitoring. Table X–1, below, which corresponds to Table 1 of paragraph (d)(3), displays the various monitoring scenarios possible under the final rule's periodic monitoring requirements. When the initial determination shows employee exposures to be at or above the action level or above the STEL, the employer is required to establish a periodic monitoring program. The 8-hour TWA monitoring is to be done every six months if exposures are at or above the action level but at or below the 8-hour TWA PEL and the STEL. The 8-hour TWA or STEL monitoring must be done every three months if the initial determination or subsequent monitoring shows results that are above the 8-hour TWA PEL or the STEL, respectively. If two consecutive subsequent monitoring results taken at least seven days apart show that exposures have decreased to or below the 8-hour TWA PEL, but above the action level, the frequency may be decreased to every six months. Eight-hour TWA monitoring may be terminated when two consecutive monitoring results taken at least seven days apart show that exposures are below the action level. STEL monitoring may be terminated when two consecutive monitoring results taken at least seven days apart show that exposures are at or below the STEL (See note to paragraph (d)(3)).

There are six possible initial determination exposure scenarios, or combinations of 8-hour TWA and short-term exposures, that determine the frequency of required monitoring. Table X–1 below lists these six exposure scenarios, along with their monitoring frequencies. As shown by Table X–1, the action level trigger largely determines whether employers must monitor employee exposure to MC. The only exception is the scenario in which 8-hour TWA exposures are below the action level and short-term exposures are above the STEL. In this case, exceeding the STEL obligates employers to monitor short-term exposures four times per year at those job locations where the STEL was exceeded, but employers are not required to monitor 8-hour TWA exposures at those job locations.

TABLE X–1.—SIX INITIAL DETERMINATION EXPOSURE SCENARIOS AND THEIR ASSOCIATED MONITORING FREQUENCIES

Exposure Scenario	Required Monitoring Activity
Below the action level and at or below the STEL	No 8-hour TWA or STEL monitoring required.
Below the action level and above the STEL	No 8-hour TWA monitoring required; monitor STEL exposures every three months.
At or above the action level, at or below the TWA, and at or below the STEL.	Monitor 8-hour TWA exposures every six months.
At or above the action level, at or below the TWA, and above the STEL	Monitor 8-hour TWA exposures every six months and monitor STEL exposures every three months.
Above the TWA and at or below the STEL	Monitor 8-hour TWA exposures every three months.
Above the TWA and above the STEL	Monitor 8-hour TWA exposures and STEL exposures every three months.

Several commenters stated that the proposal required unnecessarily frequent monitoring [Exs. 19–25, 19–26, 19–28, 19–30, 19–31, and 19–57]. Some commenters [Exs. 19–30, 19–31] said that the frequency of monitoring should be the same as that in the benzene standard (29 CFR 1910.1028 (e)(3)), since frequent monitoring does nothing to reduce or control exposures. The benzene standard requires monitoring at least every six months if employee exposure exceeds the 8-hour TWA, at least every year if exposure is at or above the action level but at or below the 8-hour TWA, and ''as necessary'' to evaluate short-term exposures. OSHA believes that MC exposure is highly variable due to the substance's volatility (vapor pressure = 350 mmHg at 20 C, compared with a vapor pressure for benzene of 75 mmHg at the same temperature) and the way that it is commonly used (e.g., in manual applications), and that reducing the frequency of exposure monitoring could therefore result in inadequate employee protection. The frequency of monitoring required by this MC standard is similar to that in other OSHA standards such as Ethylene Oxide (29 CFR 1910.1047), and is sufficient to characterize employee exposure and to evaluate the effectiveness of exposure control strategies.

The Advisory Committee on Construction Safety and Health suggested that OSHA trigger exposure monitoring by frequency of use as well as the exposure level. OSHA believes, however, that the magnitude of an employee's exposure is the appropriate determinant of monitoring frequency (and the selection of protective measures based on the results of that monitoring) because it is cumulative MC dose, not frequency of use, that determines the significance of the risk to which employees are exposed. Therefore, the Agency has not made the suggested change.

The Polyurethane Foam Association (PFA) [Ex. 19–39] questioned the necessity of requiring exposure monitoring at the action level. According to the PFA [Ex. 19–39], ''An action level of 12.5 ppm would require

that workers be monitored at a level that has only a remote health risk associated with it. The costs of such monitoring, however, would be significant.'' OSHA disagrees strongly with the PFA's analysis of the significance of the risk remaining at the action level. As discussed in the Significance of Risk and Economic Analysis sections of this preamble, only feasibility has constrained the Agency from reducing the 8-hour TWA PEL in the final rule to levels below the action level, because even at 10 ppm, the risk remaining is significant. That is, an employee exposed to an MC concentration of 10 ppm as an 8-hour TWA over a working lifetime would still be at significant risk of dying of MC-induced cancer.

Under paragraph (d)(4)(i), employers are required to perform additional monitoring when workplace conditions change or there is an indication that employee exposures may have increased. Paragraph (d)(4)(ii) requires that, where exposure monitoring is performed due to a spill, leak, rupture or equipment breakdown, the employer must clean up the MC and perform repairs and then monitor MC levels. The changes referred to in these provisions would include deliberate changes, such as a process or production change, or unexpected changes, such as a leak, rupture, or other breakdown. In the case of the latter, the employer is to perform the monitoring after taking whatever immediate action is required to clean-up or repair the equipment or source of exposure. OSHA recognizes that such occurrences can result in very high exposures. Several rulemaking participants [Exs. 19–31, 19–57, Tr. 2035, 10/14/92] stated that remonitoring is not necessary after a spill or leak since MC has a high vapor pressure, there would be no visible residual MC and no opportunity for significant exposure. However, OSHA believes that such remonitoring is an appropriate way to ascertain if proper corrective methods have been instituted and if the magnitude of an employee's exposure has changed significantly as a result of the leak or spill.

Employees are to be notified in writing of the results of exposure monitoring under paragraph (d)(5). This is to be done within 15 working days of the time the employer receives the monitoring results, and can be done either individually or by posting. When the results show that the 8-hour TWA PEL or the STEL has been exceeded, the employer must also notify employees of the corrective action being taken, and the schedule for completion of the action. This provision is effectively identical to the corresponding provision of the proposed rule.

One commenter [Ex. 19–49] argued that 15 working days is not enough time to develop corrective actions, especially where engineering controls are involved. OSHA believes that this comment misunderstands the requirement, which merely states that employers are required to ''describe the corrective action being taken * * * and the schedule for completion of this action.'' The Agency believes that 15 working days is adequate time for the employer to make a preliminary assessment that includes the immediate steps being taken to reduce employee exposure, such as utilization of air-supplied respirators, and the employer's plan for implementing permanent controls and/or work practices. This requirement is necessary to assure employees that the employer is making efforts to furnish them with a safe and healthful work environment, in accordance with section 8(c)(3) of the Act. OSHA would expect employers to update the notification when plans for permanent controls are made.

Employees or their designated representatives are provided by paragraph (d)(6) with the opportunity to observe any required monitoring of employee exposure to MC. This provision is required by section 8(c)(3) of the Act (29 U.S.C. 657(c)(3)). It was relocated to paragraph (d)(6) of the final rule from proposed paragraph (l) to consolidate all of the exposure monitoring requirements in one place. The observer, whether an employee or a designated representative, must be provided (at no cost to the observer) with any personal protective clothing or equipment required to be worn by employees working in the area that is being monitored, and must additionally comply with all other applicable safety and health procedures. These provisions of the final rule are identical to those of the proposed rule.

As noted above, OSHA received a number of comments on the monitoring provisions proposed in the NPRM. For example, Occidental Chemical Corporation requested that OSHA consider using what they termed ''exposure assessment'' rather than monitoring, testifying [Tr. 2012–2013, 10/14/92] as follows:

> [I]nstead of just looking at monitoring, which is in the middle of the process, exposure assessment looks at a basic * * * characterization: What is the characterization of the work force? What is the characterization of the workplace? What is the characterization of the contaminants in the workplace? All of that is weighed together; it's a collection of information.
>
> The next step, then, is to interpret that information and determine what are the actual exposure levels, what category would they fit into * * *. If, at that point, and this is still just a paper exercise based on that information, you * * * conclude that exposures [are] unacceptable * * * you act. You may conclude that you have insufficient data and you'd like to monitor. Or you may conclude the data are acceptable; in this case, you would act and * * * change something and go through the process again. Or, in the case they [employee exposures] are acceptable, * * * you would document that it is acceptable and then reevaluate at some regular frequency, say annually or something like that.

In response to this comment, OSHA notes that nothing in the standard prevents employers from conducting exposure assessments. Indeed, the fact that the final standard allows employers to use objective data and recent (within the past year) exposure data are both examples of the kinds of evaluation made by industrial hygienists performing exposure assessments. An employer unable to avail himself or herself of the exclusions to initial monitoring offered by the standard would logically move to the next step in the exposure assessment process: the direct monitoring of employees' exposures to MC. Thus the final rule, far from interfering with exposure assessment, actually both reflects this process and encourages employers to engage in such assessments themselves.

Paragraph (e) Regulated Areas

Paragraph (e)(1) requires employers to establish a regulated area wherever an employee's exposure to airborne concentrations of MC exceeds or can be reasonably expected to exceed either the 8-hour TWA PEL or the STEL. This paragraph was changed slightly from the proposal to clarify that OSHA is concerned with employee exposures that can reasonably be anticipated to exceed one of the PELs, rather than excessive exposures that ''may'' occur. Regulated areas can be either temporary or permanent, depending on the characteristics of a given workplace. Such areas are required by the standard to reduce employee exposures and to alert employees to those areas in the workplace that present the greatest danger of MC overexposures.

Paragraph (e)(2) limits access to regulated areas to authorized persons (a term which is defined in the definitions paragraph (b)). This provision applies when either the TWA PEL or STEL is exceeded or can reasonably be expected to be exceeded. OSHA believes that the establishment of a regulated area will help to ensure that employees are aware of areas in the workplace where MC

levels are above the 8-hour TWA PEL or STEL. OSHA believes that regulated areas are an effective means of limiting the risks of high exposures to substances suspected of being carcinogenic to humans to as few employees as possible.

Comments from Bristol-Myers Squibb [Ex. 19–14] suggested that OSHA delete the regulated area concept from the standard and replace it with a ''regulated job classification'' for jobs exceeding the PEL and a ''regulated procedure'' for procedures exceeding the STEL. This commenter's rationale was that since airborne concentrations are measured by personal monitoring and by job classification, it does not make sense to define an ''area'' of exposure. OSHA does not agree, for a number of reasons. First, in many workplaces, specific areas, such as quality control monitoring stations, mixing tanks, cutoff saw stations, spray booths, etc., are known to be associated with high levels of MC on a routine basis, and demarcating these areas protects employees by making them aware of the potential for these exposures in these locations. Second, it is standard industrial hygiene practice to use area monitoring to identify areas of exceptionally high exposures so that all non-authorized employees can be protected from overexposure. Finally, OSHA does not believe that the approach suggested by Bristol-Myers has the same potential to alert employees to the presence of high airborne concentrations that a demarcated area does, and therefore believes that the suggested change would not provide equivalent protection from overexposure.

The Laborers' Safety and Health Fund of North America [Tr. 1378–79, 9/23/92] testified that, in construction, a regulated area should be established wherever MC is used. Although there are many uses of MC on construction sites that may warrant establishing regulated areas, there are also engineering controls available (for example, portable ventilation) which may reduce employee exposures so that a regulated area would be unneccessary. OSHA believes that employers should not be required to establish regulated areas unless potential exposure levels warrant them. The Agency also believes that the employer is in the best position to determine whether the exposures from a particular MC application will warrant establishing regulated areas at a particular work site. The Advisory Committee on Construction Safety and Health also suggested that the establishment of regulated areas could replace some of the standard's monitoring requirements [Ex. 21–69]. As discussed previously, however, OSHA believes that both employers and employees benefit from knowing what exposures to MC are in a given workplace or on a specific job assignment. OSHA has therefore not revised the final rule's requirement for regulated areas in locations where exposures exceed or can reasonably be expected to exceed either or both of the PELs.

The proposal would have required that employers supply employees entering regulated areas with appropriate respiratory protection and ensure its use in such areas at all times. Several commenters [Exs. 19–25, 19–31 and 19–49] argued that respirator use in such areas should be required only if occupational exposures in such areas either exceeded the 8-hour TWA PEL or the STEL or could reasonably be expected to exceed one or both of these limits. OSHA agrees with these commenters and has revised the final rule accordingly. Paragraph (e)(3) states that employers must supply a respirator to each person who enters a regulated area, but shall require each affected employee to use that respirator only if MC exposures are likely to exceed the 8- hour TWA PEL or STEL. Thus, not all workers in regulated areas will be required to wear respirators in regulated areas at all times.

For example, under the final rule, an employer would be required to demarcate the area around a cutoff saw operator's work station in a foam blowing plant as a regulated area and to train the operator to recognize the area as regulated; however, the operator would only be required to wear a respirator in the area at times when the foam ''bun'' was coming out of the tunnel for cutting. The employer would demarcate the area because he or she recognizes, based on monitoring results for the cutoff saw operator, that this work station is one where the 8-hour TWA PEL is regularly exceeded during foam blowing operations. Because of the intermittent nature of many foam blowing operations, however, respirators would need to be worn by the operator (or other workers assisting the operator) only when foam was actually being blown. This example assumes that foam blowing operations are intermittent and that exposures at the cutoff saw would exceed the PELs only during foam blowing, although this may not be the case in all plants or at all times. In facilities where foam is blown continually and the saw operator is stationed at the end of the tunnel over the full shift, respiratory protection would likely be required to be worn in the regulated area at all times because exposures would routinely exceed the PEL in that area.

Under paragraph (e)(4), which has been added to the final rule, the employer shall ensure that, within a regulated area, employees do not engage in non-work activities which may increase dermal or oral MC exposure. This provision indicates that such non-work activities as eating, drinking, smoking, taking medication, applying lotions or cosmetics or storing such products in regulated areas are prohibited. Proposed paragraph (e)(4) has been promulgated as final rule paragraph (e)(6), as discussed below.

In addition, under paragraph (e)(5), which has been added to the final rule, the employer shall ensure that employees who are wearing respirators do not engage in activities (such as taking medication or chewing gum or tobacco) which interfere with respirator seal or performance. Proposed paragraph (e)(5) has been promulgated as final rule paragraph (e)(7), as discussed below.

Final rule paragraphs (e)(4) and (e)(5) are based on the response to NPRM Issue 41 (56 FR 57043) which indicated that OSHA was considering a provision to prohibit activities such as eating, drinking, smoking, etc. in regulated areas and asked for comments on this subject. This prohibition was supported by some rulemaking participants [Ex. 19–36, Tr. 1379, 9/23/92]. OSHA notes that it is standard industrial hygiene practice to limit such activities in regulated areas, both because employees should be aware at all times that they are working in a high- exposure area and because of health concerns. Among other things, since respirators are generally (although not always) required to be worn in regulated areas, engaging in the prohibited activities while wearing respirators might interfere with the respirator seal, placement or performance, thus reducing the effectiveness of the respirator. Furthermore, in the case of MC, smoking while being exposed to high MC concentrations (such as those prevailing in regulated areas) is particularly hazardous because MC is metabolized to CO in the body and leads to carboxyhemoglobinemia, a potentially life-threatening condition for some individuals, e.g., those with silent or symptomatic heart disease. Other OSHA health standards (e.g., asbestos, cadmium, ethylene oxide) have included similar prohibitions, and OSHA has concluded, based on the reasons discussed above and the Agency's experience with other standards, that including these

provisions in the final MC standard is appropriate.

OSHA has broadened the language and separated it into two provisions (paragraphs (e)(4) and (e)(5)) to differentiate the types of activities which would generally not be allowed in a regulated area and those which would interfere with the effective use of respiratory protection. This is consistent with OSHA's intent in this rule to allow establishment of regulated areas, but require respirator use only when the 8-hour TWA PEL or STEL is likely to be exceeded.

Paragraph (e)(6), which is essentially unchanged from the proposed provision, requires employers to demarcate their regulated areas, but it does not specify how this is to be done as long as employees are aware of the location of the area and access to it is thus minimized. Factors that the Agency believes are appropriate for employers to consider in determining how to demarcate their areas include the configuration of the area, whether the regulated area is permanent, the airborne MC concentration present in the area, the number of employees in adjacent areas, and the period of time the area is expected to have exposure levels above the PEL or STEL. Permitting employers to choose how to identify and limit access to regulated areas is consistent with OSHA's belief that employers are in the best position to make such determinations, based on the specific conditions of their workplaces. This performance-oriented approach gives employers compliance flexibility without compromising employee health.

Paragraph (e)(7), proposed as paragraph (e)(5), requires employers at multi-employer worksites who establish a regulated area to communicate information to other potentially affected employers at the worksite about the location and access restrictions pertaining to the regulated area. OSHA believes that such communication will reduce the likelihood that unauthorized persons will enter the area or that workers not involved in MC-related operations will be exposed inadvertently. Those employers whose employees are exposed to MC at concentrations above either or both of the PELs must coordinate their operations with other employers whose employees could suffer excessive exposure because of their proximity to a regulated area where MC is being used. Compliance with this provision will ensure that only those employees at multi-employer worksites who are properly authorized, trained, and equipped enter regulated areas. This provision also recognizes OSHA's awareness that, although multi-employer worksites are common in construction, they are also increasingly found in other industry sectors.

Paragraph (f) Methods of Compliance

Paragraph (f) addresses the means by which employers are to reduce employee exposures to or below the 8-hour time-weighted average (TWA) PEL or the STEL. Under paragraph (f)(1), employers are required to institute and maintain the effectiveness of engineering controls and work practices to reduce employee exposure to or below the PEL and STEL, except to the extent the employer can demonstrate such controls are not feasible. Where these measures cannot reduce the concentration of airborne MC to or below the TWA PEL and STEL, the employer is nevertheless required to implement them to achieve the lowest feasible level. The employer is required to supplement these controls with respirators where necessary to ensure that employees are not exposed to MC at levels above either the 8-hour TWA PEL or the 15-minute STEL. Section 1910.134(a)(1) of the respiratory protection standard requires respirators to be used where effective engineering controls are not feasible.

One commenter [Ex. 19–57] indicated that it should be left to professional judgment to determine whether engineering controls or respirators are the best method for protecting employees. OSHA does not agree with this comment because it fails to acknowledge the industrial hygiene hierarchy of controls, which places engineering controls ahead of administrative or personal protective equipment as methods of protecting employees from hazardous exposures. The hierarchy of controls has been established industrial hygiene practice since the 1950s and is based on the fact that engineering controls are the most effective method of protecting employees because they remove the hazard from the workplace. In contrast, respirators merely prevent employees from breathing the contaminant—it remains in the workplace air. Effective respirator use also requires constant supervision, extensive employee training and fit testing, and regular (often daily) care and maintenance of the respirator. Consequently, respirators should only be used as a means of achieving the PELs where feasible engineering controls are not available (such as in some vessel cleaning and non-stationary maintenance operations) or are not sufficient to control exposures to required levels. All OSHA substance-specific health standards have recognized and required employers to observe the hierarchy of controls, and OSHA's enforcement experience with these standards has reinforced the importance of this concept to the protection of employee health.

In the Final Economic Analysis, OSHA has described feasible control technologies for each industry affected by the final MC standard. Many employers have already implemented such controls in their workplaces and are currently achieving the MC levels required by the final rule. Examples of such feasible control strategies include dilution and local exhaust ventilation, chilling coils, magnetic pumps and magnetic floating gauges, exhausted lances for drum filling, and inline quality control sampling equipment.

OSHA acknowledges that there may be a few operations where the use of engineering and work practice controls to control exposure to MC is infeasible because exposures are highly intermittent in nature and limited in duration. In particular, OSHA is aware that the use of engineering and work practice controls to comply with the PELs is infeasible for some maintenance and repair operations and during emergency situations. Where it is infeasible to reduce workplace MC levels below the PELs through engineering and work practice controls, the employer is required to protect employees from excess exposure by providing and requiring the proper use of personal protective equipment, in this case supplied-air respirators.

As discussed in the NPRM (56 FR 57120–21), OSHA asked for comments on whether employers should be allowed to place increased reliance on the use of respirators to protect employees exposed to MC. The International Brotherhood of Painters and Allied Trades [Ex. 19–23] commented that ''[w]ith the exception of emergencies that require use of a SCBA respirator, engineering and work practice controls should be the sole method of compliance.''

In addition, the IUE [Tr. 530, 9/18/92] testified as follows:

> [R]equirements to control those exposures using engineering controls are particularly important because of the lack of adequate chemical cartridge respirators for methylene chloride. For that reason, we reject the question posed by OSHA regarding the provisions to allow greater use of respirators which came from earlier proceedings on revisions to 1910.1000.

Also, NIOSH [Tr. 884, 9/21/92] testified as follows:

> NIOSH supports the existing OSHA policy on methods of compliance, that is the

hierarchy of controls for controlling exposures to hazardous agents. Generally, this policy states that whenever feasible, engineering controls and work practices should be used to prevent exposures, and that personal protective equipment, including respiratory protection, should be used only when engineering controls are not feasible.

As discussed above, OSHA agrees with these comments. The Agency considers the use of respirators to be the least satisfactory approach to exposure control because respirators provide adequate protection only if employers ensure, on a constant basis, that they are properly fitted and worn. Also, unlike engineering and work practice controls, respirators protect only the employees who are wearing them from a hazard, rather than reducing or eliminating the hazard from the workplace as a whole. Moreover, respirators are uncomfortable to wear, cumbersome to use, and interfere with communication in the workplace, which can often be critical to maintaining safety and health. As mentioned above, OSHA has reached similar conclusions for other standards promulgated to protect employees from exposure to toxic substances. Paragraph (g) of the final standard discusses respiratory protection requirements.

The NPRM also proposed requirements for a written compliance program that would have required employers to detail their plans for implementing engineering and other controls. However, OSHA has decided to eliminate these provisions from the final rule for MC to reduce the amount of paperwork employers would be required to complete. The Paperwork Reduction Act of 1995 (PRA 95), (44 U.S.C. 3501 *et seq.*), requires agencies to minimize the paperwork burdens on the public. Preparation of written compliance plans would be classified as paperwork under the new Act. OSHA believes that the lack of a written compliance plan will not substantially reduce the effectiveness of the standard; the Agency solicits comment on this point. One of the primary benefits of a written plan is that it encourages employers to consider remedial actions soon after the standard is promulgated. For MC, however, this may not be an issue because the necessary control measures are not complex and, except for the very smallest employers, the period for compliance allowed by the standard is relatively short. Nevertheless, OSHA believes that many employers will voluntarily develop these plans because they make it easier for employers and employees to monitor progress toward compliance. OSHA will be considering including compliance plans in its standards on a case-by-case basis in future rulemakings when they are appropriate. The Agency believes that employers benefit from having a plan to meet the start-up dates, and has included examples of how this might be done in Appendix B. There were very few comments about the written compliance plan requirements, other than one stating that a written plan is reasonable but annual review and update of it is not [Ex. 19–26].

Paragraph (f)(2), proposed as paragraph (f)(1)(iv), precludes use of a schedule of employee rotation as a means of compliance with the PELs. Employee rotation reduces the extent of exposure to individual employees, but increases the number of employees exposed. OSHA is regulating MC as an occupational carcinogen, and the Agency therefore prohibits practices that would place more employees at risk. No threshold has been demonstrated for the carcinogenic action of MC, and it is therefore prudent public health policy to limit the number of workers exposed. In addition, since the dose-response relationship for MC is convex, exposure to higher concentrations for shorter periods of time is riskier than exposure to the equivalent ppm-hour concentration spread over 8 hours (when rotation is used as a method of employee exposure control, employees tend to be exposed to higher concentrations for shorter durations).

Paragraph (f)(3) requires employers to address leak and spill detection in the workplace. Employers must implement procedures to detect leaks and contain spills as well as follow appropriate methods to dispose of contaminated materials and clean-up or repair the spill or leak. These requirements were addressed in proposed paragraph (f)(1)(iii), but in the final rule have been separated out and clarified to emphasize their importance. Appendix A provides examples of procedures that would meet these requirements. Liquid MC has a high vapor pressure (350 mm Hg at 20 C). Accordingly, leaks and spills of MC-containing products could generate high airborne MC levels. The leak and spill detection program reduces the possibility of worker overexposure to MC.

Bristol-Myers Squibb (BMS) [Ex. 19–14] and Dow [Ex. 19–31] supported OSHA's performance-oriented requirement for a program to detect leaks and spills. For example, BMS stated:

[T]here are many ways in which this can be done (e.g. monitoring of tank levels, walks through areas where leaks may occur). In some cases, continuous monitoring can be done to detect leaks, however, this is not always feasible. Monitoring equipment may be very difficult and expensive to maintain and may not provide the sensitivity needed for early detection. We recommend that OSHA leave this section as it is and not specify the system or the equipment which should be used for the detection program.

Proposed paragraph (h) required employers to develop emergency plans, implement those plans when necessary, equip employees correcting emergency situations with appropriate PPE, and alert and evacuate employees potentially affected by emergencies, as necessary. In reviewing the proposed rule, OSHA concluded that the proposed requirements duplicated provisions of the Hazardous Waste Operations and Emergency Response (HAZWOPER) standard (Section 1910.120). The Agency has therefore deleted the separate MC requirement for an emergency plan, and has added a note to final rule paragraph (f)(3)(ii) which refers employers to the HAZWOPER standard for the applicable requirements.

Paragraph (g) Respiratory Protection

Paragraph (g) of the final rule addresses requirements for respiratory protection allowed to be used to comply with the MC standard. Paragraph (g)(1) requires that employers provide respirators at no cost to each affected employee, and to ensure that each affected employee uses a respirator under the following conditions:

(1) Whenever an employee's exposure to MC exceeds or can reasonably be expected to exceed the 8-hour TWA PEL or the STEL;

(2) During the time interval necessary to install or implement feasible engineering and work practice controls;

(3) In a few work operations, such as some maintenance operations and repair activities, for which the employer demonstrates that engineering and work practice controls are infeasible;

(4) Where feasible engineering and work practice controls are not sufficient to reduce exposures to or below the PELs; or

(5) In emergencies.

These limitations on the required use of respirators are consistent with OSHA's longstanding position on the hierarchy of controls in the workplace, as reflected in the respiratory protection requirements in other OSHA health standards (e.g., asbestos, §1910.1001; ethylene oxide, §1910.1047; benzene, §1910.1028; cadmium, §1910.1027) and with good industrial hygiene practice. They reflect OSHA's determination that respirators are inherently less reliable in providing protection to exposed

employees than engineering and work practice controls.

However, to reflect the changes made to the final rule's regulated area provision (paragraph (e)(1)), the final rule's respiratory protection requirements differ somewhat from those in proposed paragraph (g). In the NPRM, OSHA proposed to require that employers provide respirators in the following circumstances: (1) During the time interval necessary to install or implement feasible engineering and work practice controls; (2) in work operations, such as maintenance and repair activities, vessel cleaning, or other activities for which engineering and work practice controls are demonstrated to be infeasible, and when exposures are intermittent in nature and limited in duration; (3) in work situations where feasible engineering controls are not yet sufficient to reduce exposure to or below the PELs; and (4) in emergencies. In the final rule, another situation where respirator use is appropriate is acknowledged: whenever an employee's exposure to MC exceeds or can reasonably be expected to exceed either or both of the PELs.

The Building and Construction Trades Department, AFL–CIO, testified [Tr. 816–17, 9/21/92] that proposed paragraph (g)(1)(ii) could be interpreted by construction contractors ''as an exemption from the requirement for adopting a control strategy that places engineering and work practice controls above that of the PPE.'' In response, OSHA has revised final rule paragraph (g)(1)(ii) to clarify OSHA's intent. OSHA recognizes that it may be infeasible to control MC exposure with engineering and work practice controls during certain maintenance and repair operations, although OSHA is also aware that portable local exhaust, ''elephant trunks,'' and other means of providing ventilation to, and removing contaminated air from, process vessels and other difficult-to-reach work spaces are widely used in construction and elsewhere. The Agency also recognizes that there may be other MC-related activities where an employer could establish the infeasibility of controls, particularly where employee exposure is highly intermittent or of short duration. Accordingly, OSHA has revised proposed paragraph (g)(1)(ii) as described above. This change also addresses comments made by the Pharmaceutical Manufacturers Association (PMA) [Ex. 19–25; Tr. 1430, 9/23/92], which stated that it was infeasible for employers to protect employees during manual unloading of batch operated centrifuges and manual loading of dryers from MC exposure with engineering and work practice controls. The PMA suggested that OSHA revise proposed paragraph (g)(1)(ii) to include those loading and unloading activities in the list of operations allowed to protect affected employees through the use of air-supplied respirators. However, OSHA included examples in the proposal only to provide a general indication of the situations where the Agency would accept the use of air-supplied respirators in lieu of engineering and work practice controls. OSHA believes that the examples suggested by the PMA are too narrowly focused for inclusion in such a list. It would not be possible for OSHA to enumerate in the final rule all of the workplace-specific operations where engineering and work practice controls may be infeasible. Therefore, in accordance with longstanding OSHA practice, employers claiming that engineering and work practice controls are infeasible must establish infeasibility on an objective basis.

Other commenters were concerned about requiring respirators during emergency escape situations, noting the time involved in donning a respirator in an emergency. The Dow Chemical Company stated ''Dow believes the respiratory protection requirements for emergency escape are excessive. For the short period of time it takes to escape a release of MC, considering the minor acute effects of the material, it is excessive to require, as a minimum, a gas mask with an organic vapor canister'' [Ex. 19–86].

Similarly, comparing escaping right away or first finding a respirator and then escaping during an emergency situation, Occidental Chemical testified [Tr. 2041, 10/14/92]:

> Methylene chloride is not incapacitating so the goal should be to escape as fast as possible not trying to find a device—and it may be close, it may be further—and then put it on, which could take a minute or so, 30 seconds or a minute, and then decide about escape. That whole process becomes much longer. So I'm not advocating we don't have escape respirators, just that the process should be, escape should be the number one priority.

OSHA agrees that escape is the first priority for employees exposed to MC in an emergency situation. Furthermore, the Agency has determined, in general, that the ready availability of escape respirators is essential to ensure that employees are able to escape safely. To that end, emergency plans must provide for fast access to escape respirators where the potential for emergency exposure situations has been identified by the employer. In addition, employees must be trained to don those respirators properly and quickly and to recognize any foreseeable situations where taking the time to obtain and put on their respirators would significantly reduce their ability to escape or where they can safely escape an emergency situation without using respirators. OSHA recognizes that immediate escape is not always possible, so respirators are needed to protect those employees while they are still in the exposure area.

Paragraph (g)(2), proposed as paragraph (i)(1)(ii), requires employers to determine that any employee required by this standard to wear a supplied-air respirator in the negative pressure mode or a negative-pressure respirator for escape purposes is medically fit to use such a respirator. This provision has been changed from the proposal to recognize that medical fitness for respirator users under this standard is appropriate only for negative-pressure respirators or those operated in that mode. This change will assist employers to direct their medical surveillance resources effectively. In addition, in keeping with the greater flexibility provided by this standard to employers in selecting an appropriate health care professional, paragraph (g)(2) uses the final rule's language, ''Physician or other licensed health care professional,'' in lieu of the proposal's exclusive use of ''physician.''

Paragraph (g)(3), proposed as paragraph (g)(2), requires employers to select appropriate atmosphere-supplying respirators from among those listed in Table 2 (Table 1 in the proposed rule), which sets forth the minimum requirements for respiratory protection and is unchanged from the proposal. Employers may use respirators approved for a higher level of protection in lower concentrations of MC. Employers are required to select atmosphere-supplying respirators that have been approved by NIOSH under the provisions of 42 CFR Part 84. Also, employers must select vapor canisters which have been approved by NIOSH when they provide gas masks with organic vapor canisters for use in emergency escape. The final rule differs from proposed paragraph (g)(2) in that it does not require employers to give employees who cannot wear negative pressure air-supplied respirators or who cannot wear a negative pressure (organic vapor canister) during an emergency escape the option of wearing a respirator with less breathing resistance. OSHA believes that the respirators required by the final rule will not strain an employee's respiratory system during such use.

Issue 30 (56 FR 57042) asked if the proposed respirator selection table

(Table 1 in the proposal) appropriately regulated the choice of respirators. Several commenters suggested changes. For example, Abbott Laboratories [Ex. 19–29] suggested that OSHA allow the use of a continuous flow air-supplied hood or helmet for exposures up to 5,000 ppm instead of 625 ppm of MC. On the other hand, the Laborers' Health & Safety Fund of North America [Ex. 19–36] suggested that OSHA require employers to provide positive pressure SCBAs or airline positive- pressure full facepieces with auxiliary escape for all exposures over 25 ppm, instead of allowing any flexibility, in keeping with NIOSH recommendations for respiratory protection against carcinogens. The Advisory Committee on Construction Safety and Health [Ex. 21–69] recommended that respirators, when used, be pressure-demand, supplied air respirators with an auxiliary self-contained breathing apparatus, because of MC's fast cartridge/canister breakthrough and the lack of effective end-of-service-life indicators.

OSHA is currently in the process of developing a final standard to revise its general respiratory protection provisions in 29 CFR 1910.134. Until that rulemaking is completed the Agency will continue to rely on NIOSH's Assigned Protection Factors (APF) for determining the types of respirators required for protection to airborne concentrations of MC. The APF for continuous flow hoods/helmets is 25 in the NIOSH Respirator Decision Logic. The maximum specified use concentration for a respirator is generally determined by multiplying the exposure limit, in this case 25 ppm, by the protection factor, which is 25; therefore, these hood/helmets could be used only up to 625 ppm of MC. Using the same decision logic, OSHA believes that adequate protection can be provided by the respirators described in Table 2 when they are used under appropriate exposure conditions.

Some commenters questioned the reliability of atmosphere-supplying respirators. For example, in the furniture stripping industry commenters noted that MC could cause damage or potential damage to the hoses, the plastic lens, and the gasket of the facepiece of air line respirators or other kind of respirators, resulting in inadequate protection. [Ex. 19–11; Tr. 348–9, 9/17/92; Tr. 2146–7, 10/14/92; Tr. 2505–2506, 10/15/92]. In addition, the Occidental Chemical Corporation [Tr. 2115, 10/14/92] noted that none of the manufacturers contacted had hoses resistant to MC-induced corrosion. The Agency acknowledges that MC may damage respirator components, if the MC is left on them for extended periods of time. However, existing §1910.134 (f) already requires employers to inspect respirators frequently and to maintain respirators at their original effectiveness. In addition, MC does not damage rubber components which are available. Most importantly, if feasible engineering controls and work practices are not available, properly utilized air-supplied respirators are the only way to protect employee health from significant risk.

Issue 30 also requested information on the circumstances under which air-purifying respirators may be used. Dr. Morton Corn of Johns Hopkins University testified [Tr. 2352, 10/15/92] that ''* * * with the current state of knowledge and the breakthroughs I indicated, [allowing gas masks with organic canisters for emergency escape only] is a prudent restriction at this time.''

Several commenters disagreed with Dr. Corn and remarked that there are some situations where air-purifying respirators may be appropriate in addition to emergency situations, and recommended that OSHA expand the provision to allow the use of air-purifying (filter) respirators. For example, Occidental Chemical testified [Tr. 2113–4, 10/14/92] as follows:

> Transportation workers who make deliveries in trucks can have intermittent exposure to methylene chloride inside the truck and, if you set the PEL too low, and in that emergency situation * * * you can't have engineering controls on some types of trucks, especially if they are rented. You ought to allow the use of respirators in that case; it's a very short type exposure, goes in, takes the drum out, and then gets back in the truck. Now it may be possible to schedule operations in certain industries where the PEL is exceeded for short periods of time. Filter cartridge respirators could be used to protect the worker during the short periods of time without the use of cumbersome supplied-air respirators. Of course, you have to have changes in the regulated areas in the rules also if you're going to allow the use of respirators where you have intermittent exposures above the PEL.
>
> And a short breakthrough time does not mean a respirator is useless. If you use the NIOSH calculations, at 200 parts per million which might be typical of paint stripping, you ought to have about 118 minutes worth of time before you get breakthrough; and that may be enough in paint stripping operations.

Similarly, Bristol-Myers Squibb stated that air-purifying respirators may be appropriate in certain circumstances [Ex. 19–14]:

> Based upon the scientific information now in the record, BMS requested that OSHA consider allowing chemical cartridge air-purifying respirators for specific types of activities (lower MC concentrations, shorter durations).
>
> Organic vapor cartridges can be used for protecting employees against exposures to MC where using an air-supplied respirator would not be feasible due to costs or process (e.g. multiple working areas). Only air-supplied respirators should be used for operations involving the need for extended wear (e.g. greater than several hours).

The Eastman Kodak Company [Ex. 102] also requested that OSHA allow air-purifying respirators ''in circumstances where their effectiveness can be adequately demonstrated, engineering controls are not feasible and supplied-air respirators are impractical or potentially unsafe. OSHA also should permit the use of half mask respirators'' [Tr. 1196–7, 9/22/92]. In addition, Kodak described specific situations where it believed the use of air-purifying respirators was appropriate:

> The use of air-supplied respirators must be an essential component of the exposure-control strategies for both the Roll Coating Division and the Dope Department. Moreover, the evidence demonstrates that air-purifying canister or cartridge-type respirators may appropriately be used in some operations, such as certain dope maintenance tasks. The use of air-purifying respirators is appropriate where: (1) air-supplied respirators or other controls are impractical or potentially unsafe, (2) personal monitoring of employees is conducted regularly, (3) the extremes and conditions of the exposure potential are well characterized, and (4) used cartridges are tested after use to verify the absence of unacceptable breakthrough. It is essential that OSHA permit the use of air-purifying respirators under these circumstances so that Kodak can control employee exposure when engineering and work practice controls and air-supplied respirators are infeasible, ineffective or potentially unsafe.

OSHA considered including a provision in the final rule to allow exceptions for the use of air-purifying respirators in limited circumstances where very tight control of the respirator program is implemented. However, the Agency has rejected this alternative for several reasons. First, the record strongly supports the inadequacy of such respirators for employee protection. Consequently, the use of air-purifying respirators should only be considered when the use of air-supplied respirators presents major disadvantages. Second, a program to use air-purifying respirators would have to be very detailed and be tailored to a specific workplace. It would be difficult, if not impossible, to list all of the relevant factors and criteria for such a program in the regulatory text, which must necessarily be appropriate to apply to many workplaces. (Below, OSHA discusses the Agency's variance procedures, which employers wishing to use air-purifying respirators may use to apply for a variance.)

While there may be circumstances when the use of filter respirators may seem preferable to the use of atmosphere-supplied respirators, OSHA has concluded, as a general matter, that air- purifying respirators do not provide sufficient, consistent, and reliable protection to employees exposed to MC. In support of this conclusion, NIOSH testified as follows [Tr. 887–89, 9/21/92]:

At the request of OSHA, NIOSH has completed an in-depth study of the breakthrough characteristics of MC for organic vapor respirator cartridges and canisters under a variety of test conditions. This work was undertaken to determine MC breakthrough time for commercially available, organic vapor respirator cartridges and canisters. Several MC challenge concentrations were studied, ranging from 50 ppm to 1,000 ppm. As received cartridges and canisters were tested at equivalent flow rates of 64 Lpm through the respirator and at both 50% and 80% relative humidities (RHs). Breakthrough times were determined for individual cartridges and canisters, as well as stacked cartridges. The results of this study show rapid breakthrough of MC for organic vapor cartridges even for low concentrations of MC (e.g., 5 ppm breakthrough at approximately 30 minutes for 50 ppm challenge concentration and 80% RH). Appendix D is a detailed report of this study. At 125 ppm challenge concentration, 5 ppm breakthrough, and 80% RH, one brand of cartridge showed breakthrough times of approximately 40 minutes. The same brand of chin-style canister, that contains approximately 2 and ½ to 3 times more sorbent than two cartridges (i.e., two cartridges per respirator) showed breakthrough times of approximately 100 minutes when tested at the same conditions. The same brand of front- or back-mounted canister, that contains approximately 10 times more sorbent than two cartridges, showed breakthrough times of approximately 600 minutes. Based on the results of this study, NIOSH supports the OSHA proposal to require the use of air-supplied respirators in lieu of air-purifying respirators. However, because of the potential carcinogenicity of MC, NIOSH continues to recommend only the most protective positive-pressure respirators as noted previously.

The NIOSH study indicated that MC quickly penetrates organic vapor cartridges (in a fraction of a typical work shift), contrary to the assertions of Occidental Chemical and the other commenters mentioned above. Larger canisters, which contain greater amounts of absorbent, last longer, but are still effective for less than a work shift (except for very large canisters). Another problem with organic vapor cartridges and canisters is that MC migrates through the absorbent even when the respirator is not being used. This further decreases the breakthrough time and raises the possibility that the employee will be exposed to significant concentrations of MC. Also, humidity decreases the amount of MC collected by the absorbent.

Another problem with air-purifying respirators in the case of MC is this substance's poor warning properties, which mean that workers will not be able to smell or sense the presence of MC when breakthrough occurs. OSHA believes that employees wearing air-purifying respirators could easily have a false sense of security and be lulled into believing that they were being protected against MC when it could already have broken through the absorbent. Accordingly, OSHA has concluded that it would be inappropriate to allow broad-scale use of air-purifying respirators because of MC's quick breakthrough time and its carcinogenic health effects.

Employers who believe that the use of filter respirators is appropriate for their operations may apply for a permanent variance from the requirements of paragraph (g)(3) of this section, pursuant to the authority granted by § 6(d) of the Occupational Safety and Health Act and the procedures set out in 29 CFR part 1905. In particular, an applicant would need to establish that the use of filter respirators in a specific workplace would provide employee protection equivalent to that which would be provided through compliance with final rule paragraph (g)(3). As discussed below, the respirator program, procedures, and data needed to support the use of such respirators under a variance are extensive.

A successful variance application for an exception that would allow air-purifying respirators would have to address a number of the characteristics that employers such as Eastman-Kodak [Ex. 102] indicate they have undertaken with regard to the use of such equipment. For example, extensive exposure monitoring would have to be done to accurately characterize employee MC exposure levels. Furthermore, the breakthrough time for MC when used in the airborne concentrations expected in the workplace would have to be known, and cartridges would have to be changed before employees are unacceptably exposed. The program would have to be carefully monitored by a trained and experienced individual such as a certified industrial hygienist or the equivalent. Finally, the respirators would have to be appropriately fit tested for each affected employee. For all of the reasons stated above, OSHA has determined that the interests of employee protection will be best served by requiring all employers, except those whose respiratory program, procedures, and exposure data can support a variance request, to provide their employees with the respirators shown in Table 2.

Paragraph (g)(4), which is identical to the proposed (g)(3), requires employers to implement a respiratory protection program in accordance with 29 CFR 1910.134 whenever respirator use is required by this standard. The respiratory protection program must include basic requirements for proper selection, fit, use, training of employees, cleaning, and maintenance of respirators. For employers to ensure that employees use respirators properly, OSHA has found that the employees need to understand the respirator's limits and the hazard against which it is providing protection in order to appreciate why specific requirements must be followed.

Paragraph (g)(5) (effectively identical to proposed paragraph (g)(4)) requires that employers allow employees wearing respirators to leave the regulated area to readjust the respirator facepiece to their faces for proper fit. In addition, employers must permit employees who wear respirators to leave the regulated area to wash their faces as necessary to prevent skin irritation associated with respirator use. These requirements encourage the proper use of respirators by authorizing employees to take specific actions that ensure the effective functioning of respirators and reduce the likelihood that employees will experience adverse side effects from wearing respirators.

Paragraph (g)(6), which is essentially the same as the corresponding proposed paragraph, addresses situations where employers provide gas masks with organic vapor cartridges for purposes of emergency escape. If gas masks are used, the canisters are to be replaced before the gas masks are returned to service. This requirement is necessary because actual MC exposures during emergencies are generally not known, so the expected service life of the canister cannot be determined. In addition, the migration of MC within the canister after emergency exposure further reduces the amount of useful life remaining, posing exposure risks for subsequent users.

Paragraph (g)(7) addresses respirator fit and is essentially identical to the corresponding provision of the proposal. It requires the employer to ensure that each respirator issued is properly fitted and has the least possible facepiece leakage.

Under paragraph (g)(7)(ii), the employer must perform qualitative or quantitative fit testing initially and at

least annually thereafter for each employee wearing a negative pressure respirator, including those employees for whom emergency escape respirators of this type are provided. A note has been added to this provision to indicate clearly that the only supplied-air respirators to which this provision would apply are SCBAs operated in the negative pressure mode and full facepiece supplied-air respirators operated in negative pressure mode. Quantitative fit testing relies on objective data generated by measurements of facepiece seal leakage, in contrast to qualitative fit testing, which is based on subjective observations made by the respirator wearer. Many commenters expressed a preference for quantitative fit testing over qualitative fit testing. For example, Newport News Shipbuilding (NNS) [Ex. 19–37, p. 2] stated: ''Quantitative respirator fit testing is the method of choice. At NNS we use quantitative fit testing exclusively, as this method is more definitive than qualitative fit testing and provides a record of the fit test.'' The Shipbuilders Council of America [Ex. 19–56, p. 11] took the same view.

Several commenters noted the importance of proper selection and fit testing of respirators [Exs. 19–12, p. 3; 19–31, pp. 15–17; 19–71, p. 4]. Dr. David Newcombe of the Department of Environmental and Health Sciences at The Johns Hopkins University testified as follows:

> I think that's [quantitative fit testing] a very important parameter because, first of all, respiratory protection when it's required takes a reasonable amount of time to ensure that the individual is properly fitted so that the mask fits if that's the piece that's going to be used and is protective against the substance that you're protecting against and, in addition, I think it's important to note that some people may have deformities that cause a poor fit and, therefore, don't protect and so I would think that you have to have a careful assessment of the type of respiratory protection you're going to use, its fit in a single individual as well [Tr. 800, 9/18/92].

In most cases, OSHA has determined that positive pressure respirators are the respirators of choice for MC exposure, especially loose-fitting models such as hoods or helmets; for these respirators, fit testing is generally not needed. However, for those situations where negative pressure respirators are used, fit testing is needed. Qualitative or quantitative fit testing allows the employer to test various respirators on the employee until the appropriate fit is identified and selected for the employee.

Paragraph (h) Protective Work Clothing and Equipment

Paragraph (h) requires that, where needed, employers provide and ensure the use of the appropriate protective clothing and equipment. The requirements for protective work clothing and equipment were separated from proposed paragraph (g) (respiratory protection and personal protective equipment) and moved to paragraph (h) to facilitate compliance. Proposed paragraph (g)(6) was effectively identical to this paragraph.

Protective clothing used during exposure to MC, such as gloves or aprons, must be resistant to MC. The Building and Construction Trades Department, AFL–CIO [Tr. 832, 9/21/92] suggested that OSHA codify NIOSH's recommendations for protective clothing materials suitable for use with MC. MC is a constituent of so many different products that a codification of guidance regarding appropriate protective clothing would be unwieldy and unlikely to be complete. Further, the continual formulation and reformulation of MC products virtually ensures the early obsolescence of any protective clothing guidelines.

Therefore, OSHA believes that it is appropriate for paragraph (h) to set general criteria and for the Agency to adopt the NIOSH recommendations in a nonmandatory appendix so employers will have more detailed guidance and so OSHA can update that guidance, without rulemaking, as advances in PPE technology cause existing guidance to become outdated. As discussed above, this performance-oriented approach reflects OSHA's belief that employers are in the best position to select protective measures that are tailored specifically to the needs of their workplaces.

Paragraph (h) requires the employer to provide all necessary protective clothing and equipment at no cost to the employee and to launder, repair, replace and safely dispose of that clothing and equipment. The final rule is performance-oriented so the employer has the flexibility to provide only the protective clothing and equipment necessary to protect employees in each particular work operation from MC exposure. The generic requirements for PPE in the general industry, construction, and shipyard standards also apply to PPE for MC, except where a specific provision of the MC standard applies.

Paragraph (i) Hygiene Facilities

Paragraph (i) of the final rule establishes requirements for hygiene facilities in establishments where it is reasonably foreseeable that an employee's eyes or skin may contact solutions containing 0.1 percent or greater MC. Although such provisions were not part of the proposed rule, OSHA requested comment on the appropriateness of including such requirements in Issue 38 (56 FR 57122). Specifically, the Agency requested comment on the appropriateness of including requirements for quick-drench showers and eye-wash facilities in the final rule. OSHA described quick-drench showers as,'' * * * showers that could drench an employee with piped-in water applied with force,'' and eyewash facilities as devices ''that could flush the eyes repeatedly with a great amount of water.'' In response to comments, described below, the Agency has decided that it is not necessary to specify in the final rule when showers and eyewash facilities are required to protect employees from skin or eye contact with MC, because employers are in the best position to determine whether the MC used in their establishments meets the 0.1 percent cutoff specified in this provision and whether contact of the eyes or skin with MC can reasonably be foreseen.

Paragraph (i)(1) requires employers to provide conveniently located washing facilities appropriate to removing MC if it is reasonably foreseeable that the employee's skin may contact a solution containing 0.1 percent or greater MC through splashes or spills. MC can be absorbed into the body through skin contact (percutaneous absorption), which would add to the dose employees receive via inhalation and thus increase the risk of cancer and other adverse health effects. However, MC is not a corrosive chemical, and, if left on the skin for short periods, is not likely to cause long-term or irreversible damage. Therefore, it is important that employers make provisions to remove MC from the skin of employees quickly, although immediate drenching is not usually required. This requirement has been stated in performance-oriented language in the final rule to allow employers to determine what type of washing facilities are needed and at what distance from affected employees. This provision thus recognizes that employers in some facilities, such as furniture stripping shops where a thick MC gel is used that may burn the skin on contact, employers need to position washing facilities in closer proximity to affected employees than is the case where less hazardous solutions of MC are used. OSHA believes that this requirement of the final rule strikes the

right balance between employee protection and employer flexibility by ensuring that washing facilities for the skin will be available and appropriately placed in workplaces where such contact is likely.

MC splashed into the eyes will cause irritation if the MC is not promptly washed out, and immediate flushing is therefore required. Paragraph (i)(2) requires employers to provide appropriate eyewash facilities within the immediate work area for emergency use if it is reasonably foreseeable that an employee's eyes will contact solutions containing 0.1 percent or greater MC through splashes or spills.

Existing OSHA requirements at § 1910.141 and § 1926.51 establish generic provisions for hygiene facilities but do not focus on MC-specific situations. Existing § 1910.151(c) and § 1926.50 (g) require employers to provide suitable facilities for quick-drenching or flushing of body and eyes within the immediate work area for immediate emergency use, when the body or eyes may be exposed to injurious corrosive materials. However, because MC is not classified as a corrosive material, these existing requirements would not apply. Thus the final rule's performance-oriented requirements will provide guidance to employers about what facilities and access distances are appropriate for conditions in their workplaces. In addition, Appendix A provides examples of both washing facilities and eyewash facilities that would satisfy this requirement.

The response to Issue 38 emphasized the need for eyewash and shower facilities [Exs. 19–37, 19–56; Tr. 2644–2645, 10/16/92; Tr. 1942–1943, 9/24/92]. For example, PRMA testified [Tr. 348, 9/17/92] that MC splashes happen ''almost every day'' in furniture stripping workplaces.

Commenters also addressed the health effects associated with such accidental exposures. The Amalgamated Clothing and Textile Workers Union testified [Tr. 1825, 9/24/92]:

> I would advocate including it [the provisions for showers and eyewash facilities]. It [methylene chloride] has skin effects. Anyone who's ever stripped paint can tell you about what it's like to get it on their skin or their eyes. So it's very important to be able to irrigate an affected area promptly.

One means to provide protection from prolonged skin or eye exposure to MC from accidents is to specifically require quick-drench showers and eyewashes. The NPRM sought comments on whether or not the final rule should require employers to provide quick-drench showers and eyewash facilities. Many commenters recommended that the final rule contain such provisions [Exs. 19–15; 19–36; Tr. 532, 9/18/92; Tr. 1380, 9/23/92; Tr. 2352–53, 10/15/92]. For example, PRMA [Ex. 19–11] favored a requirement for eyewash/ quick drench facilities, stating as follows:

> An eyewash station is a safety device that should be required in any work environment where there is the possibility of splashing chemicals into ones eyes. Quick drench showers are also a safety device that should be standard equipment in every facility. MC paint removers are one of the few paint removers that are easily rinsed from one's eyes.

The Dow Chemical Company commented [Ex. 19–31]:

> Washing facilities are always a good idea when working with any material, however, it is not always necessary to have quick-drench showers, etc. Incidentally, quick-drench showers do not deliver water ''applied with force.'' They work on a deluge system delivering a large amount of water to wash off the material, not force it off. Installing showers and eyewash fountains in all workplaces may not be economically feasible. There are other systems such as water hoses, portable eye-washes, etc. that work effectively for MC. MC is a material that, in some cases, may be painful if held against the skin for a period of time, but is not eye nor skin nor life threatening. Therefore, an immediate shower is not required.

OSHA agrees that quick drench and eyewash facilities are effective means for treating employees who have been accidentally exposed to MC by spills or splashes. However, the Agency agrees with Dow Chemical that quick drench showers are not the only means to ensure proper first aid treatment for MC exposure due to accidental splashes or spills and believes that other types of washing facilities can also provide effective treatment for accidental exposure.

In some cases, the availability of a hose attached to a potable water supply would enable employers to provide effective first aid treatment. This could be an especially effective means of protection at a construction worksite. Several commenters [Ex. 19–23, 19–38; Tr. 859, 9/21/92] agreed that construction employers should have potable water at the worksite in case of accidental exposure. For example, the Building and Construction Trades Department, AFL–CIO, testified [Tr. 817, 9/21/92]:

> The standard does not address the need for available hygiene facilities. Since methylene chloride can damage the skin and eyes and potable water is often in limited supply on construction sites, the requirement for potable washing areas must be clearly stated in the standard. Potable water supplies should be of sufficient volume to provide at least 15 minutes of continuous flushing.

The Occupational Health Foundation testified that the MC standard should require that hygiene facilities be provided within a reasonable distance at construction worksites [Tr. 858–859, 9/21/92]:

> Unlike in a lot of other work sites where at least there's a sink nearby, in construction you really need to specifically mandate that provision to be sure that there's going to be water anywhere remote, you know, within a reasonable distance to the work site.

Issue 38 also requested information on the extent to which MC-exposed employees are already provided with quick drench showers and eye wash facilities. Several commenters described workplaces that have emergency shower or eyewash facilities in place. The United Automobile, Aerospace and Agricultural Implement Workers of America (UAW) testified [Tr. 1942–1943, 9/24/92] ''[t]here are a lot of showers and eye washes in areas where you have open-top chemicals or use of chemicals.'' In addition, the Occidental Chemical Corporation testified [Tr. 2159, 10/14/92]:

> . . . we conducted a survey of our customers that were not CMA and not NACCD members recently and asked them questions like that. We have some information on that. It doesn't necessarily mean that we hit a large percentage of our methylene chloride customers, though.
> . . . we have safety shower[s] and eyewash[es] [in our plants], certainly. We have . . . recommendations on it and we certainly follow the ANSI standards on it.

Newport News Shipbuilding (NNS) and the Shipbuilders Council for America both commented [Exs. 19–37 and 19–56] that ''[p]rocedures at NNS now require eyewash units. For the most part we use portable (5 gallon) units. Plumbed combination units would be better.'' The National Tank Truck Carriers, Inc. also indicated that their facilities are already equipped with emergency showers [Tr. 1750–51, 9/24/92].

With regard to the proximity of employees to emergency showers and eye washes, commenters and testimony indicated that, depending on the work operation, shower facilities have been installed as close as eight feet or as far away as 100 feet. For example, the J. M. Murray Center, testified [Tr. 1047–48, 9/21/92] that they have both eye washes and showers that are ten to twelve feet from the employees.

The Polyurethane Foam Association (PFA) testified [Tr. 1630, 9/23/92] that the proximity of shower facilities and eye washes depends on the plant and

operation within the plant, stating as follows:

> We've got methylene chloride in bulk storage area and we also use it at the foam machine. The total range from those things that you might be would be anywhere from eight feet to may be 60 feet. And I'm guessing at the 60 feet. That, again, is specific for those plants that I am responsible for. There are 80-some-odd plants out there, and I can't speak for that particular physical setup in each one of those plants.

The PFA further stated in its post hearing comment:

> Eye wash and drench showers are available in the production areas. These are located within 10 to 15 feet of the work stations, such as near bulk storage tanks and the mixing head, where a higher risk of employee exposure exists. Hygiene facilities may be 50 to 75 feet away from other work areas [Ex. L–100A].

The Eastman Kodak Company testified [Tr. 1259, 9/22/92] that emergency eye-wash and quick-drench showers are available in their workplaces, and that such stations are between 50 and 100 feet from all work areas where exposure to chemicals may occur.

Striptech International, which advocated requirements for pressure showers and eyewash facilities where workers are exposed to MC [Ex. 19–15], also testified that hygiene facilities are not readily accessible in the aircraft paint stripping industry [Tr. 1834–35, 9/24/92]:

> I've heard people ask about deluge in eye wash. Does it exist in aircraft maintenance hangars? Yes, it surely does; but you also have to look at where they normally are. They're normally on the walls. When a man or a lady is on top of an aircraft, on the tail of an aircraft, they may be nine stories in the air. If they get methylene chloride in their eyes or really a bad shot of it, they've got to come down nine stories and may be cross a 400 to 600-foot-long hangar to get to it. Deluge showers, yes; all aircraft people have them. Are they readily accessible? No.

It is important for the employer to evaluate the potential hazard posed by the particular use of MC and to provide appropriate washing facilities within a reasonable distance and eyewash facilities within immediate reach. In addition, employers are required to provide employees who are at risk of skin and/or eye contact with MC with appropriate protective clothing and eye protection. Portable eyewash units, which would significantly reduce any delay in irrigating the eyes, are available and can be located within easy access distance of affected employees. As described above, access to washing facilities should be quick, but immediate showering is not generally necessary to address the MC skin hazard. Therefore, an employee stripping an airplane would likely have time to get to the showers located along the walls of the hangar to wash MC from the skin. (Note: Some paint stripping compounds do contain corrosives, and immediate access to quick-drench facilities is essential in such cases.) Based on a review of the rulemaking record, the Agency has determined that performance-oriented provisions for hygiene facilities are reasonably necessary to supplement the other requirements of the final rule and has promulgated paragraph (i) accordingly.

Paragraph (j) Medical Surveillance

Section 6(b)(7) of the OSH Act requires that, where appropriate, occupational health standards shall prescribe the type and frequency of medical exams or other tests to be made available, by the employer or at the employer's cost, to exposed employees in order to determine if the employee's health is being adversely affected by exposure to workplace hazards.

A medical surveillance program that complies with paragraph (j) enables the employer to:

(1) Determine if an employee has an underlying health condition that places the employee at increased risk from the effects of exposure to MC;

(2) detect, insofar as possible, early or mild clinical conditions arising as a result of MC exposure, so that appropriate preventive measures can be taken;

(3) identify any occupational diseases that occur as a result of MC exposure; and

(4) help to evaluate possible trends in the incidence of these diseases.

The most serious health effect that may result from MC exposure is cancer. Although a medical surveillance program cannot detect MC-induced cancer at a preneoplastic stage, OSHA anticipates that, as in the past, methods for early detection and treatments leading to increased survival rates will continue to evolve. Moreover, the cardiovascular disease, central nervous sytem and dermal irritation effects caused by MC exposure can already be detected at early or mild stages by medical surveillance provisions such as a medical history and a medical exam. MC has not been tested adequately for the full range of possible health effects that may result from exposure, so it is also not presently possible to identify all diseases that may be associated with exposure to MC. The specific level of protection afforded the worker by the final standard cannot be predicted with certainty, although the risk of exposure for those effects that have been identified are significant, and the record shows that reducing the exposure of employees will significantly reduce that risk. An important goal of the medical surveillance program is to provide information related to the adequacy of the PELs for MC by documenting the health condition of exposed employees, particularly in the area of carcinogenicity.

Several rulemaking participants [Exs. 19–31, 19–83, Tr. 1802–3, 9/24/92] stated that the proposed medical surveillance provision should be deleted from the final rule because it would not detect employee exposure to harmful levels of MC. In addition participants contended [Ex. 19–83, Tr. 458, 9/17/92] that the medical surveillance provision is too expensive and burdensome. OSHA has determined that the medical surveillance program required by the final rule is reasonably necessary for the protection of workers. In particular, medical surveillance will directly benefit workers with cardiovascular disease, central nervous system effects, and dermal irritation. These conditions can be detected by the medical surveillance program required by this paragraph of the final rule, and the detection of such conditions can, in turn, alert the employer to potential overexposures to MC in the workplace and to the need to limit MC exposures for certain employees with underlying heart disease or other conditions.

In addition, by increasing the performance orientation of the rule, OSHA has minimized the costs of medical surveillance while maintaining its effectiveness. For example, the final rule leaves the content of laboratory surveillance for individual employees to the discretion of the physician or other licensed health care professional. Also, the requirement for a physical examination has been tailored to the age of the employee, so that employees younger than 45 generally receive an exam only every three years, instead of annually. The medical surveillance program also will aid in the evaluation of cancer incidence in the workplace and temporal trends therein.

Paragraph (j)(1) specifies the circumstances under which employers must provide medical surveillance for employees who are or may be exposed to MC. Under paragraph (j)(1)(i), employers must make medical surveillance available to all employees who are exposed to MC at or above the action level for 30 days or more in any year or above either of the PELs for at least 10 days in any year. This provision is effectively identical to the corresponding provision of the

proposed rule. Also, this requirement is consistent with the approach taken by OSHA in the benzene standard (29 CFR 1910.1028). OSHA recognizes that the health effects associated with MC exposure are, in general, the result of chronic exposures to MC. Accordingly, employees exposed only for a few days in any year will be at relatively low risk of developing MC-induced disease. The exposure duration thresholds in the final rule will thus enable employers to focus valuable medical resources on high-risk employees.

Some commenters were concerned about the use of the PELs and action level as triggers for medical surveillance. The Building and Construction Trades Department, AFL-CIO [Tr. 817, 9/21/92] was concerned that this provision would preclude medical surveillance for some employees with MC exposures that exceeded the PELs on fewer than 10 days in a given year but who might nonetheless be at risk of adverse health effects. OSHA has determined that employees who have been identified by a physician or other licensed health care professional as being at risk for cardiac disease or some other serious MC-related health condition and who are exposed to MC at levels that exceed the PELs on fewer than 10 days in any year should have the option of participating in a medical surveillance program. Accordingly, paragraph (j)(1)(ii) has been added to the final rule. This provision states that medical surveillance must be provided to any employee (1) who is exposed above the 8-hour TWA PEL or STEL for any time period, and (2) who has been identified by a physician or other licensed health care professional as being at risk from cardiac disease or from some other serious MC-related health condition, and (3) who requests inclusion in the medical surveillance program. As noted in the Health Effects section, above, OSHA is concerned that any MC exposure above either of the PELs could exacerbate cardiac problems. This paragraph enables such high-risk employees to participate in a medical surveillance program.

Under paragraph (j)(1)(iii), appropriate surveillance is required to be made available to employees exposed in an emergency regardless of the airborne concentrations of MC normally present in the workplace. Where very large amounts of materials are kept in a sealed system, routine exposure may be very low. However, rupture of the container might result in extremely high MC exposures. Thus, it is appropriate for employers who have identified operations where there is a potential for an emergency involving MC to plan ahead so that emergency medical surveillance would be available if needed. This provision is effectively identical to proposed paragraph (i)(1)(iii).

Proposed paragraph (i)(1)(ii) would have required that the employer have the examining physician or other licensed health care professional determine if affected employees are physically fit to wear respirators. OSHA has placed this requirement with the other respiratory protection provisions in paragraph (g) of this final rule.

Paragraph (j)(2) requires that employers offer examinations without cost to employees, at a reasonable time and place, and without loss of pay. OSHA believes that this provision is necessary to encourage employees to participate in the medical surveillance program. Final rule paragraph (j)(2), which is essentially identical to proposed paragraph (i)(2), is also consistent with other OSHA health standards and with provisions contained in the OSH Act.

Paragraph (j)(3) requires that all medical procedures be performed by or under the supervision of a physician or other licensed health care professional, defined as ''an individual whose legally permitted scope of practice (i.e., license, registration, or certification) allows him or her to independently provide or be delegated the responsibility to provide some or all of the health care services required by paragraph (j) of the standard.'' The proposal required that all medical procedures be performed only by or under the supervision of a physician. Only one commenter [Ex. 19–31] specifically supported this provision.

OSHA has long considered the issue of whether and how to identify the particular professionals who are to perform the medical surveillance required by its health standards. The Agency has determined that other professionals who are licensed under state laws to provide medical surveillance services would also be appropriate providers of such services for the purposes of the MC standard. The Agency recognizes that the personnel able to provide the required medical surveillance may vary from state to state, depending on state licensing laws. Under the final rule, an employer has the flexibility to retain the services of a range of qualified licensed health care professionals, thus potentially reducing costs, increasing flexibility, and allowing employers to identify those professionals, who may not necessarily be physicians, with the greatest expertise in diagnosing and treating occupational diseases. In future rulemakings, OSHA may attempt, with the cooperation of interested stakeholders, to specify which licensed health care professionals are the most appropriate to perform each of the diagnostic, therapeutic, medical management and other services required by the Agency's standards.

Paragraph (j)(4) of the final standard addresses when medical examinations and consultations are to be provided.

Initial surveillance. Under paragraph (j)(4)(i), initial medical surveillance must be provided before an employee's initial assignment to work in an area where they would be exposed to MC or by the start-up dates described in paragraph (n)(2)(iii) of the final MC standard, whichever is later. The employer need not repeat equivalent medical surveillance if it has already been provided within the past 12 months. OSHA's requirement for a preplacement examination is intended to determine if an individual is at increased risk of adverse effects from exposure to MC. It also establishes a general baseline for future reference. The provisions of final rule paragraph (j)(4) are effectively identical to those in proposed paragraph (i)(3), except that the proposed rule did not take into account medical surveillance provided prior to the effective date of this section. In the preamble to the NPRM (56 FR 57124), OSHA stated that it was considering a provision that would give employers credit for medical examinations provided within one year of the standard's effective date. The Agency requested comment on the usefulness of such a provision. Commenters [Exs. 19–31, 19–55b, 19–83] supported such a provision. In particular, Dow Chemical [Ex. 19–31] stated ''[i]f this is not done this section will be unfair to those employers who have on-going health surveillance programs.'' OSHA agrees with these commenters and has promulgated the final rule accordingly.

Periodic surveillance. Paragraph (j)(4)(ii) addresses periodic medical surveillance. OSHA proposed to require annual medical surveillance for all affected employees. In the final rule, this has been changed so that the employer is required to update the medical and work history for each affected employee every year but must only provide physical examinations on a schedule that varies with the age of the employee. For affected employees 45 years of age or older, the physical examination must be conducted every year. For employees less than 45 years of age, the examination need only be done every three years.

OSHA differentiated these groups of employees in an effort to target surveillance resources effectively. The probability of developing heart disease (which can be exacerbated by MC exposure) increases as employees age. Age 45 is a rough approximation of the point at which medical professionals would have heightened concern for cardiac effects. In other words, it is generally more likely that employees 45 years and older would experience the adverse cardiac effects of MC exposure. Three-year intervals between physical examinations for workers younger than 45 seemed the proper interval to balance the conservation of valuable medical resources and the provision of a medical surveillance program that is useful for detecting adverse MC health effects. The annual updates on medical and work history will enable the physician or other licensed health care professional to identify those individuals for whom more frequent examinations would be appropriate.

To a lesser extent, this would be true for the detection of MC-induced cancer as well. Although MC-induced cancer cannot currently be detected at the pre-neoplastic stage, early detection of cancer generally increases the survival rate, so it is important to include employees exposed to MC in a medical surveillance program that may detect tumors. Since any cancers caused by MC are more likely to be found in older employees and employees exposed to MC for longer durations, it is reasonable to concentrate medical surveillance resources on older employees.

The main goal of periodic medical surveillance for workers is to detect adverse health effects at an early, and potentially still reversible, stage. The intervals chosen based on the age of the employee are consistent with this purpose and with other OSHA health standards. The Agency believes that these periodic surveillance requirements strike a proper balance between the need to diagnose health effects, such as cancer, at an early stage, thus increasing the effectiveness of medical intervention, and the expectation that a limited number of cases will be identified through the surveillance program. This approach decreases the cost burden of surveillance by lengthening the period of time between examinations for younger employees who have fewer years of exposure and thus have a lower risk of adverse health effects.

Termination of employment or reassignment. Paragraph (j)(4)(iii) requires the employer to provide medical surveillance when an employee terminates employment or is reassigned to an area where exposure is consistently at or below the action level and the STEL. The termination examination need not be conducted if medical surveillance has been performed within the past six months. This requirement reduces the likelihood that an employee who terminates employment has an active, but undiagnosed, disease related to his or her MC exposure. In the NPRM, OSHA had proposed that the termination examination be performed unless medical surveillance had been conducted on that employee within the past three months. The Motor Vehicle Manufacturers Association [Ex. 19–42] requested that the exam should only be required if the employee has not had a medical exam within six months of termination or reassignment, instead of three months as had been proposed. The MVMA stated that ''six months is adequate and consistent with other OSHA health standards (Cadmium, Sec. 1910.1027(l)(8)). We see no contribution to reducing employee risk from examining such employees at an earlier date, especially since the exposure to methylene chloride has been removed.'' Upon reconsideration of the issue, OSHA has adopted this suggestion in the final rule.

The Agency requested public comment on whether continued annual surveillance should be offered to employees who have left employment, retired, or transferred to other areas within the employer's operations. Such an approach would be consistent with the requirement in the Benzene standard (29 CFR 1910.1028), which makes medical surveillance available to certain employees who have been exposed to benzene during their employment with their current employer. Several commenters [Exs. 19–31, 19–38, 19–42, 19–48, 19–55b, 19–58] stated that there should be no medical surveillance after an employee leaves a job in an exposure area or for employees previously exposed to MC. In particular, Dow Chemical [Ex. 19–31] stated: ''[W]e do not believe that the employer should be responsible for continued medical surveillance for employees who leave MC exposure areas * * *. [T]he continued surveillance does nothing more than divert occupational medical resources from more important work.'' Taking a different view, the IUE [Tr. 533, 9/18/92] testified that formerly exposed retirees should be included in the medical surveillance program. They also stated that retirees, presently employed workers formerly exposed to MC in previous jobs, and workers relocated to nonexposed areas should be included in the medical surveillance program. The ACTWU agreed, testifying [Tr. 1763–1764, 9/24/92] that employees who continue to work for the same employer after their exposure to MC is terminated should be entitled to participate in the medical surveillance program.

OSHA has decided that it would be inappropriate to include retirees and other formerly exposed employees in the medical surveillance program. A major value of medical surveillance is to detect the acute heart disease and CNS effects associated with MC exposure. Workers no longer exposed to MC, or retirees, would be at much less risk of experiencing these effects.

Additional surveillance. Paragraph (j)(4)(iv) requires employers to provide additional surveillance when the physician or other licensed health care professional recommends that it be provided. This may be warranted, for example, for an employee who is under 45 years of age but has a health condition that requires surveillance more frequently than every 3 years. Inclusion of this provision in the final rule will ensure that all employees receive the most appropriate level of surveillance for their particular health situation. The proposed provision was essentially identical.

Paragraph (j)(5) of the final rule, like paragraph (i)(4) of the proposal, establishes the requirements for the content of medical exams. This provision requires a comprehensive medical and work history, a physical examination, laboratory surveillance, and any additional information determined to be necessary by the physician or other licensed health care professional. The language in the proposed rule, which was similar, has been revised for clarity and to provide guidance about what constitutes adequate medical surveillance. For example, the final rule addresses medical and work history in greater detail than the proposal because, in some cases, three years may elapse before a subsequent physical examination is provided. On the other hand, the specific content of the physical examination and laboratory surveillance has been left largely to the discretion of the physician or other licensed health care professional.

Paragraph (j)(5)(i) requires that a comprehensive medical and work history be obtained from each participating employee. This paragraph requires a medical evaluation that includes a comprehensive medical and work history with special emphasis on neurological symptoms, skin conditions, history of hematologic or liver disease,

signs or symptoms suggestive of heart disease (angina, coronary artery disease), risk factors for heart disease, MC exposures, and the work practices and personal protective equipment used to control exposures. OSHA has included an example of a medical and work history format that would satisfy this requirement in non- mandatory Appendix B of the standard. The proposed provision required a comprehensive or interim medical and work history with emphasis on neurological symptoms, mental status, and cardiac health. Final rule paragraph (j)(5)(i) has been revised to indicate clearly what is required.

The medical and work history component of the initial medical evaluation will assist the physician or licensed health care professional in identifying pre-existing conditions that might place the employee at increased risk when exposed to MC. It also establishes a health baseline for future monitoring. The subsequent annual updates will identify changes in neurological symptoms, skin conditions or cardiac health, and, in combination with laboratory analyses and information on exposure history, may provide early warnings of MC toxicity. The information derived from a medical evaluation assists the physician or other licensed health care professional in distinguishing between MC-related effects and those effects that are unrelated to MC exposure. This information is particularly important because the health effects associated with MC exposure are not unique to such exposure. For example, the proposed requirement to assess mental health status has been eliminated from the final rule because no specific correlation has been demonstrated between mental health status and MC exposure.

Paragraph (j)(5)(ii) requires that the extent and nature of the required physical examinations be determined by the physician or licensed health care professional based on the health status of the employee and analysis of the medical and work history for that employee. The standard also requires that the examiner give particular attention to the lungs, cardiovascular system (including blood pressure and pulse), liver, nervous system and skin. Proposed paragraph (i)(4)(ii) specifically would have required that the examination address the lungs, liver, nervous system and breast. OSHA has determined that, in order to indicate clearly that the physician or licensed health care professional should assess the potential cardiac health impacts of MC, the medical exam should give attention to the cardiovascular system, blood pressure and pulse. In addition, the Agency has decided that, because of the skin irritation effects of MC, it is necessary to include evaluation of the skin in the medical exam.

Two hearing participants [Tr. 803, 9/18/92; Tr. 2434–35, 10/15/92] testified that men over 40 years old should be given electrocardiograms (ECGs), which should be repeated every 1 to 3 years. OSHA is not requiring ECGs because there is no evidence in the record that associates specific changes in ECGs with MC exposures. However, the physician or licensed health care professional has the discretion to order an ECG for any employee where it is deemed appropriate.

Proposed paragraph (i)(4)(iv) also required the physician to make a determination of any reproductive difficulties of the employee. Vulcan Chemicals [Ex. 19–48] and Organization Resources Counselors (ORC) [Ex. 19–51] commented that the evidence for a relationship between reproductive effects and MC exposure did not warrant inclusion of such a provision in the final rule. OSHA agrees with these commenters that the evidence associating MC exposure and specific reproductive health effects is sparse. Therefore, the Agency has not included reproductive effects in the list of effects the physician or other licensed health care professional should focus on. However, the Agency will continue to monitor the literature to determine if future evidence indicates that inclusion of this provision is warranted.

Two commenters [Exs. 19–28, 19–42] stated that the breast examination requirement should be eliminated from the final rule because breast exams would be highly unlikely to identify effects related to exposure to MC. In the proposal OSHA placed attention on the breast because of concern raised by the increased number of breast tumors in the rat bioassay. Upon further consideration, OSHA has dropped the requirement for breast exams. The Agency notes that rats are particularly sensitive to mammary tumors and it is unclear that humans have similar risks of developing breast cancer after exposure to MC. The Agency remains concerned about the potential for MC carcinogenicity evidenced by the rat mammary tumors, however, and has relied, in part, on mammary tumor data in identifying MC as a cancer hazard.

In final rule paragraph (j)(5)(iii), laboratory surveillance of employees is to be conducted as the examining physician or licensed health care professional determines to be necessary and appropriate, based on the employee's health status and the medical and work history. This is a more performance-oriented provision than the corresponding provision of the proposed rule. The proposal would have required several specific laboratory tests, while the final rule leaves laboratory test requirements to the discretion of the physician or other licensed health care professional. Non-mandatory Appendix B includes guidance regarding the types of tests that may be appropriate.

Some commenters [Exs. 19–28, 19–42, 19–48, 19–49] stated that COHb levels, which had been included among the tests in the NPRM, are not a good measure of toxic exposure to MC. In particular, the MVMA [Ex. 19–42] stated that it is difficult to determine the COHb level attributable to MC exposure for employees who are smokers or who may have other exposures to CO. Several other participants [Exs. 19–25, 19–57, 19–83 and Tr. 1438, 9/23/92] suggested that COHb testing should be done only after over-exposure to MC, such as after an emergency. The Laborers Health and Safety Fund [Tr. 1386, 9/23/92] testified,

> [W]e're not convinced that that's [COHb monitoring] an appropriate and accurate measure of exposures, given other sources of carbon monoxide on construction sites as well as the issue of smokers versus non-smokers.

However, the Department of the Army [Ex. 19–55b] suggested that COHb levels are a more cost-effective measurement of the oxygen-carrying capacity of blood than a complete blood count. Similarly, the California Department of Health Services [Ex. 19–17] requested that references to COHb testing be moved from the appendix to the regulatory text.

COHb levels greater than 3% can exacerbate angina symptoms, decrease exercise tolerance and increase risks for myocardial infarctions (heart attacks) in susceptible individuals. COHb concentrations can also be used as a rough estimate of worker exposure to MC (taking into consideration smoking behavior, time since exposure, and exposure to other CO sources) to calibrate personal MC monitoring measurements. Before- and after-shift COHb determinations can be useful in correlating recent MC exposures with COHb levels. The Agency is not requiring COHb testing, however, because confounding factors, such as smoking or exposure to a CO source, can reduce the usefulness of the results of the tests and, in addition, COHb does not measure a health effect per se but is instead a surrogate measure of MC exposure. However, COHb testing may

be clinically important in the evaluation of a symptomatic worker and therefore remains an option for the physician or other licensed health care professional to pursue. Exposure monitoring (see paragraph (d) of the final rule) must be performed to quantify an employee's exposure to MC.

In the comments received subsequent to publication of the ANPR for MC [Exs. 10–3, 10–10, 10–28], several industry commenters indicated that urine analysis, liver function tests and chest X-rays are commonly performed as part of the medical surveillance programs of these companies. OSHA believes that annual urine analysis or chest X-ray would not be relevant to detection of MC-related health effects. Liver function tests have also been evaluated for inclusion as a requirement in the medical surveillance provision. As discussed above in the Health Effects section, animal studies and human clinical studies show an association between chronic MC exposure and some changes in liver enzymes, particularly after high exposures or doses of MC for prolonged periods of time. The changes in liver enzyme levels after MC exposure are not consistent in the human clinical studies, however, and in general, changes in liver enzymes are not specific or unique to MC exposure. Therefore, the Agency believes that it should be left to the physician's or other licensed health care professional's discretion to determine if laboratory analysis of liver enzymes is warranted.

Several commenters [Exs. 19–11, 19–26, 19–42, 19–48, 19–55b] agreed that routine use of all of the tests included in the proposal would not be appropriate or necessary for the detection of MC-related health effects. The Agency also sought comments on the inclusion of other medical tests in the final MC rule. Two commenters [Exs. 19–31, 19–48] stated that a complete blood count was not necessary because the results of this test may not correlate with MC overexposure. In particular, the Dow Chemical Co. [Ex. 19–31] commented that a complete blood count is not necessary because blood cell volume and hemoglobin findings would suffice. OSHA has reevaluated the utility of the proposed tests and has decided that leaving laboratory surveillance to the discretion of the physician or licensed health care professional is more cost-effective than the approach taken in the proposal and will not negatively impact worker health.

In paragraph (j)(5)(iv), the final rule requires the medical surveillance program of the employer to include any other information or reports the physician or other licensed health care professional determines are necessary. This is to ensure that a complete medical profile is available to the physician or licensed health care professional to make decisions regarding the employee's health and exposure status. This provision is essentially identical to that proposed.

Paragraph (j)(6) of the final rule describes the required contents of emergency medical surveillance. The proposed rule did not specify what elements should be included in an emergency medical exam. The final rule clarifies that emergency medical surveillance should include any appropriate emergency treatment and decontamination of the exposed employee, a comprehensive physical exam, an updated medical and work history, and laboratory surveillance, if needed.

The Dow Chemical Company [Ex. 19–31] commented that employees exposed to MC during an emergency should not automatically be included in the regular medical surveillance program. Instead, this commenter argued that only those components of a medical examination that are appropriate in a given situation should be conducted. OSHA believes that it is important for an employer to provide medical examinations and appropriate follow-up to employees exposed to MC during an emergency. After considering the issue and comments raised during the rulemaking, the Agency agrees with Dow that employees exposed to MC during an emergency should not necessarily be enrolled in the continuing medical surveillance program provided to employees routinely exposed to MC. To that end, OSHA has added language to the final rule that clearly indicates what emergency medical surveillance is required. OSHA believes that final rule paragraph (j)(6) allows the employer appropriate flexibility, while at the same time ensuring that those employees exposed to MC during an emergency receive appropriate medical surveillance.

Paragraph (j)(7) requires the employer to provide medical surveillance services, in addition to those specified in final rule paragraphs (j)(5) and (j)(6), when the physician or other licensed health care professional determines that they are necessary. Compliance with this requirement will ensure that the information needed to evaluate the effects of MC exposure on employees is available. This provision is essentially the same as proposed paragraph (i)(5).

Paragraph (j)(8) requires that the employer provide the physician or other licensed health care professional with (1) a copy of the standard, including the relevant appendices; (2) a description of the affected employee's past, current, and anticipated future duties as they relate to the employee's MC exposure; (3) a description of former, current or anticipated exposure levels (including the frequency and exposure levels anticipated to be associated with emergencies), as applicable; (4) a description of any PPE that the employee must use or will use, such as respirators; and (5) information from any previous medical examinations that would not otherwise be available to the examining physician or other licensed health care professional. OSHA has determined that the physician or other licensed health care professional needs the above-listed background information in order to place the information derived from medical surveillance in the proper context. For example, a well-documented exposure history assists the physician or other licensed health care professional in determining whether an observed health condition may be related to MC exposure. It also helps this individual to determine if the results of medical surveillance indicate a need to limit an employee's occupational exposure to MC. This paragraph is essentially the same as proposed paragraph (i)(6).

Paragraph (j)(9) of the final rule requires employers to ensure that the examining physician or other licensed health care professional provides the employer and the affected employee with a written opinion that addresses (1) the physician's or other licensed health care professional's opinion as to whether the employee has any detected medical condition that would place the employee at increased risk of material health impairment as a result of exposure to MC; (2) any recommended limitations on the employee's exposure or use of personal protective clothing or equipment and respirators; (3) a statement that the employee has been informed of the potential carcinogenicity of MC, the risk factors for heart disease, and the potential for exacerbation of underlying heart disease associated with exposure to MC; and (4) a statement that the employee has been informed of the results of the medical examination and any medical conditions related to MC exposure that require further explanation or treatment.

The physician or other licensed health care professional must provide copies of the written medical opinion to the employee and the employer within 15 days after completion of the evaluation of medical and laboratory findings, but no later than 30 days after the medical examination. This

requirement was included to ensure that the employee and the employer have been informed of the above-mentioned results of the medical examination in a timely manner. This requirement differs slightly from that in proposed paragraph (i)(7)(i). Instead of the physician providing a copy of the written medical opinion to the employer, who then provides a copy to the employee, the final rule requires the physician or other licensed health care professional to supply a copy of the written medical opinion directly to both the employer and the employee. In addition, the time allowed for providing the opinion has been changed to recognize that time may be needed to receive and evaluate laboratory or other medical findings. The Agency believes that notifying both the employer and affected employees of the MC-related results of the medical surveillance at the same time is an efficient approach to disseminating this information to the appropriate parties. Providing copies of the same written opinion both to the employer and the employee ensures that the employer is aware of any factors that may influence work assignments or choice of personal protective equipment.

OSHA has added a requirement to the final rule that the physician or other licensed health care professional inform the employee of the carcinogenic and cardiac effects of MC to reinforce the information on MC's serious health effects that was transmitted during training. The Agency believes that this reinforcement will help to ensure that employees are aware of the potential effects of MC and take appropriate precautions when using this toxic substance.

OSHA received several comments on different aspects of paragraph (j)(9). For example, the UAW [Tr. 1884, 9/24/92] testified that the written opinion transmitted to the employer by the physician or other licensed health care professional should only state the limitations on the employee's exposure or use of respiratory or other personal protective equipment recommended by the physician or other health care professional, and should not include the medical or other reasons behind the recommended limitations.

OSHA agrees with the UAW that it is important to protect the privacy of employees enrolled in medical surveillance programs. Consequently, OSHA health standards have traditionally included a statement to the effect that no findings or diagnoses should be included in the physician's written opinion that are unrelated to occupational exposure. This requirement is intended both to protect the employee's privacy and to encourage employees to participate in the employer's medical surveillance program. The restriction on what may be revealed in the written opinion appears in the final rule as paragraph (j)(9)(ii), and is intended to apply to all of the information provided in the physician's or other licensed health care professional's written opinion, including that related to recommended limitations.

The MVMA [Ex. 19–42] and ORC [Ex. 19–57] stated that the proposed 15-day requirement for providing the employer with a copy of the written opinion should be 15 days from the physician's or other licensed health care professional's receipt of the test results rather than 15 days from the date of the examination. The Agency agrees and, as described above, has changed the requirement so that the written opinion must be provided within 15 days of completion of evaluation of medical findings, but not more than 30 days after the examination. OSHA believes that this strikes the proper balance between allowing sufficient time for the physician or other licensed health care professional to evaluate any laboratory findings while still providing the information to the employer and the employee in a timely manner.

Newport News Shipbuilding [Ex. 19–37] and the Shipbuilders Council of America [Ex. 19–56] stated that the written opinion should require only that employees be notified of abnormal test results, not normal results. In response to these comments, OSHA notes that such a provision would actually require many physicians and other licensed health care professionals to change their current practice because it would require them specifically to delete normal results from printouts of laboratory and other findings. Such reports routinely display all results, both normal and abnormal, for a given individual. In addition, OSHA believes that employees benefit from knowing which of their blood parameters and other test results are normal and which are abnormal. OSHA does not believe that requiring medical personnel to increase the amount of paperwork they perform is a good use of medical resources, and has therefore not revised the final rule to respond to these comments.

Under paragraph (j)(9)(ii) of the final rule, the physician or other licensed health care professional must exclude findings or diagnoses that are unrelated to MC exposure from the written opinion provided to the employer. As discussed above, OSHA has included this provision in the final rule to reassure employees participating in medical surveillance that they will not be penalized or embarrassed by the employer's obtaining information about them that is not directly pertinent to MC exposure. The above provisions are identical to those in proposed paragraph (i)(7)(ii). A note has been added to the final rule that states that the written opinion developed to comply with the MC standard may also contain information related to other OSHA standards. For example, an employer whose employees are enrolled in medical surveillance due to their exposure to benzene, formaldehyde *and* MC could receive a single, consolidated written opinion that addressed findings related to all three substances. This performance-oriented provision could result in reduced paperwork burdens for employers.

NPRM Issue 3 solicited input regarding whether the Agency should add a provision for Medical Removal Protection (MRP). Medical removal protection encourages employee participation in (and therefore increases the effectiveness of) the medical surveillance program by ensuring that reporting symptoms or health conditions to the physician or licensed health care professional will not result in loss of job or pay. Several rulemaking participants expressed support for the inclusion of MRP in the final rule [Exs. 19–23, 19–38; Tr. 1787, 9/24/92; Tr. 1802, 9/24/92; Tr. 1869, 9/24/92; and Tr. 1883, 9/24/92]. For example, the Amalgamated Clothing and Textile Workers (ACTWU) [Tr. 1793, 9/24/92] testified that OSHA should require MRP based on clinical judgment, as OSHA allowed in the final rule for formaldehyde (29 CFR 1910.1048). They also stated that they believed it was critical to have a medical removal protection provision in the MC standard in order to ensure worker participation. Mr. Frumin of the ACTWU testified as follows [Tr. 1792–1793, 9/24/92]:

> As I say, the problems that employers, physicians and, for that matter, OSHA confront in trying to assure the integrity of medical surveillance programs are not limited to a particular substance. They deal with the general perception—these problems arise from the general perception of workers, which is widespread through industry, that if they submit to a medical examination and it's not confidential, and employers could get the results of the medical findings, that health problems may result in some negative action.
>
> You have a symptom-based medical surveillance program, at least for the non-cancer effects. And if workers are supposed to report the types of symptoms, for instance, that Dr. Soden was looking for, shortness of breath, things of that nature—and they're